PNC
Piano nazionale per gli investimenti complementari al PNRR
Ministero dell'Università e della Ricerca

FIT4MEDROB

D3.4

HTA AND SUSTAINABLE BUSINESS MODELS OF THE ROBOTIC SOLUTIONS #1

Piano Nazionale Complementare (PNC) – Decreto Direttoriale n. 931 del 6 giugno 2022 – Avviso per la concessione di finanziamenti destinati ad iniziative di ricerca per tecnologie e percorsi innovativi in ambito sanitario e assistenziale

Project identifier: PNC0000007

Start date: 01/12/2022

Duration: 44 months

Website: www.fit4medrob.it

Editor: Giuseppe Turchetti (SSSA)
PIs: L. Trieste (SSSA), M. Orso (SSSA), G. Manfroni (SSSA), N. Bellini (SSSA), L. Cinquini (SSSA), A. Tenucci (SSSA), G. Turchetti (SSSA), J. Vitale (UCBM), L. Pecchia (UCBM)

Due date of deliverable: 31/05/2024
Actual submission date: 20/09/2024
Version: 1.1

DISSEMINATION LEVEL OF DELIVERABLE		
PU	Public, fully open, e.g. web	**X**
CO	Confidential, restricted under conditions set out in Partners Agreement	

PNC
Piano nazionale per gli investimenti complementari al PNRR
Ministero dell'Università e della Ricerca

HISTORY OF CHANGES

VERSION	SUBMISSION DATE	CHANGES
1.0	31/05/2024	First release
1.1	20/09/2024	Revised executive summary following external reviewers' suggestions.

TABLE OF CONTENTS

1. EXECUTIVE SUMMARY

In order to favour the introduction and adoption of robotic solutions in the rehabilitation procedures, it is necessary to demonstrate - in an HTA perspective - their value with respect to the economical, organizational, usability/acceptability, ethical/legal implications, and to design business models/business plans that are sustainable both for technology producers and for technology adopters/payers.

The current deliverable is the first in a series of three deliverables focusing on the Health Technology Assessment (HTA), early HTA (eHTA) and sustainable business models-business plan of robotic rehabilitation solutions. As the inaugural deliverable, it describes the general principles and methods of HTA, eHTA, and criteria for developing sustainable business models and plan for the technologies tested, integrated, and developed within Fit4MedRob, concurrently with the administration of the first clinical protocols.

The next deliverable in the series (D3.4.2 HTA and Sustainable Business Models of the Robotic Solutions #2, due on month 30) will summarize the outcomes of eHTA and HTA for specific robotic rehabilitation solutions based on the clinical and non-clinical data collected at both the early and final stages of the clinical trials, respectively. At that stage, it will be possible to design concrete business models and plans for the sustainable adoption and diffusion of rehabilitation robotic technologies. In the third and last deliverable (D3.4.3 HTA and Sustainable Business Models of the Robotic Solutions #3, due on month 44), other than the presentation of an updated and refined analysis of data coming from the clinical studies, clear recommendations and a practical, and tested, set of tools for the design and running of HTA and eHTA studies, and for the definition of sustainable business models-business plans will be described, useful for all those who will innovate in the field of robotic rehabilitation technological solutions.

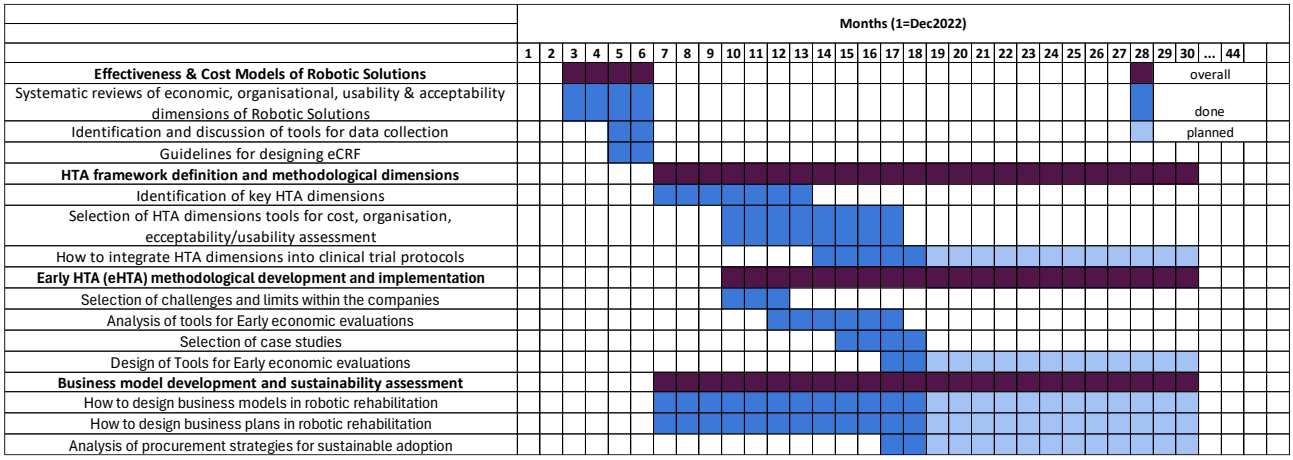
The current report is divided in three parts: the first is focused on HTA, with the presentation and discussion of its rationale, its difference with respect to pharmacoeconomics, its perspective, its technical tools, its dimensions (the economic, the acceptability/usability, the organisational, the legal/ethical ones). Moreover, a description of the first applications of this approach is presented, describing the way in which we included the HTA dimensions in the protocols of some trials that in the last months have been designed and submitted to Ethical Committees.

The second part is focused on early HTA (eHTA), with the presentation and discussion of its objectives, its specificities, its perspectives, its technical tools. This approach will be particularly useful for supporting the R&D process of brand new or low TRL technologies.

The third part is focused on business models, with the presentation and discussion of their aims, their role, the articulation and the single phases that have to be managed in order to design the plan. Moreover, in an inductive perspective approach, a first analysis of the more frequent business models adopted by companies working in the sector has been run and interesting feedback have been derived, useful for the structuring of the sustainable business models that we will propose in Fit4MedRob project. Finally, considering the sustainability dimension of the business models, we started to analyse the topics to take into account with respect to the pricing strategies and the reimbursement constraints of rehabilitation procedures that use robotic technologies.

A section with the list of references and an appendix with the details of the analysis that, following an inductive approach, we run in order to collect data, evidence and information useful for defining how to design the business plan, closes the report.

The following diagram provides an overview of the activities carried out within the project timeline, focusing on the implementation of HTA and eHTA methodologies, business model development, and data collection through clinical trials. Given the multidisciplinary nature of the Fit4MedRob initiative, our work has been closely interconnected with other key activities. Hence, the **progress of this task is fully in line with the expected timeline.**



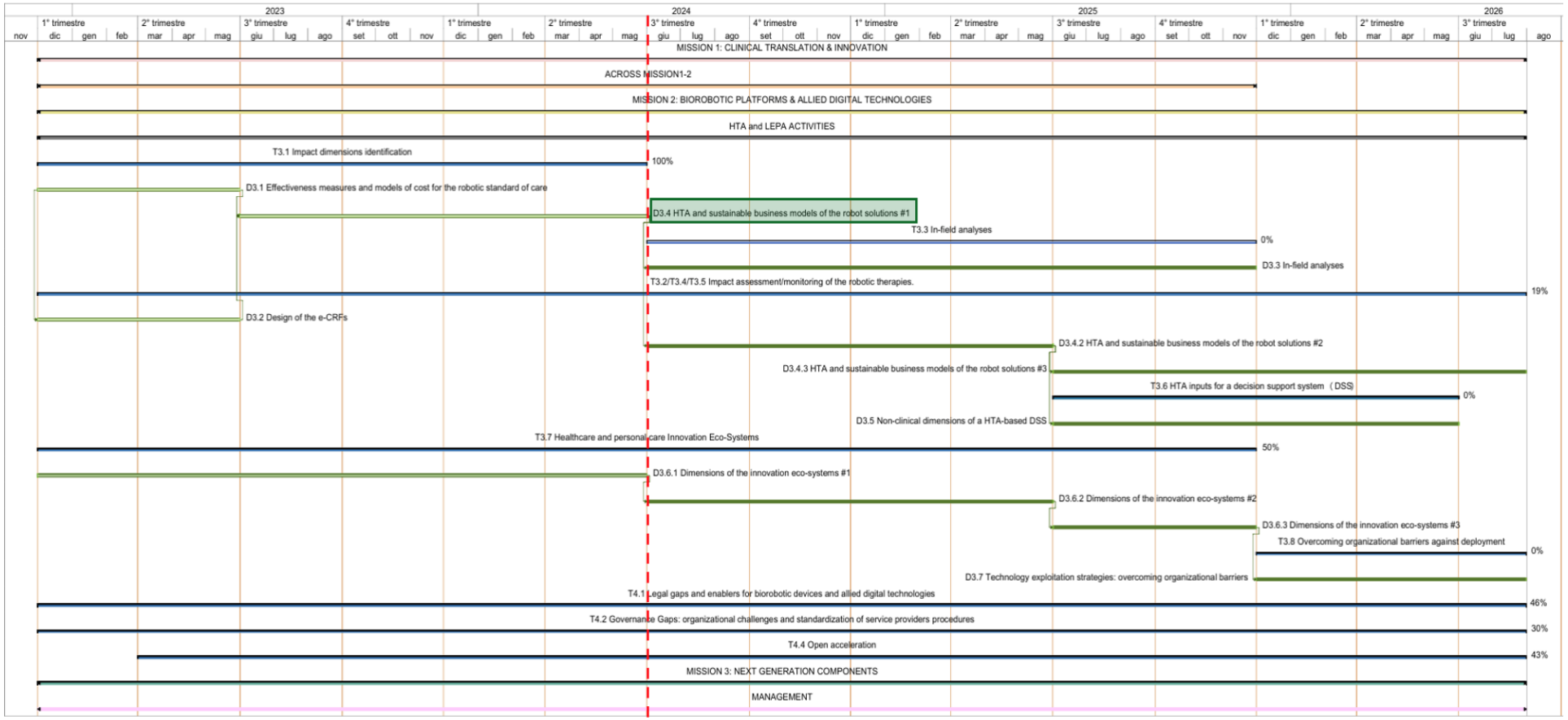
Specifically, we have collaborated with the **clinical research teams** to align methodologies and data collection strategies. This collaboration involved the identification and selection of HTA dimensions tools for the assessment of economic, organisational, usability and acceptability of robotic solutions. This activity allowed to define how to standardise data collection across trials, ensuring consistency in this assessment activity. Through these shared tools, we contribute to the design and execution of clinical protocols, enabling the evaluation of real-world applications of robotics in rehabilitation settings. Moreover, the interaction with **both the clinical and technological teams** has helped in the selection of the relevant parameters to include in the design of informatic tools to run early Health Technology Assessment analyses.

In parallel, we have identified, analysed, discussed how to design business models and business plans for robotic solutions. This activity has benefited, and even more will benefit in the next months, from the interaction with the **legal and policy teams** of the project to incorporate multi-level governance considerations and reimbursement models into our analysis of sustainable business strategies. The expertise in regulatory frameworks and healthcare financing is instrumental in shaping our approach to business model development. Moreover, the reimbursement policies, legal constraints, and institutional frameworks are taken into account and inform our evaluation of economic sustainability, ensuring that the proposed solutions align with existing healthcare structures and funding mechanisms.

These interactions allow us to bridge the gap between clinical effectiveness, financial sustainability, and regulatory feasibility, reinforcing the holistic assessment of robotic rehabilitation technologies within Fit4MedRob.

In the next months we will build on these activities to refine the HTA and eHTA tools and the sustainable business models. In particular, the interaction with the clinical teams and the integration of our activities will be even more intense in the running of the clinical trials (Gantt chart below).

GANTT CHART


2023
2024
2025
2026
1° trimestre
2° trimestre
3° trimestre
4° trimestre
nov dic gen feb mar apr mag giu lug ago set ott nov dic gen feb mar apr mag giu lug ago set ott nov dic gen feb mar apr mag giu lug ago set ott nov dic gen feb mar apr mag giu lug ago
MISSION 1: CLINICAL TRANSLATION & INNOVATION
ACROSS MISSION1-2
MISSION 2: BIOROBOTIC PLATFORMS & ALLIED DIGITAL TECHNOLOGIES
HTA and LEPA ACTIVITIES
T3.1 Impact dimensions identification
100%
D3.1 Effectiveness measures and models of cost for the robotic standard of care
D3.4 HTA and sustainable business models of the robot solutions #1
T3.3 In-field analyses
0%
D3.3 In-field analyses
T3.2/T3.4/T3.5 Impact assessment/monitoring of the robotic therapies.
19%
D3.2 Design of the e-CRFs
D3.4.2 HTA and sustainable business models of the robot solutions #2
D3.4.3 HTA and sustainable business models of the robot solutions #3
T3.6 HTA inputs for a decision support system (DSS)
0%
D3.5 Non-clinical dimensions of a HTA-based DSS
T3.7 Healthcare and personal care Innovation Eco-Systems
50%
D3.6.1 Dimensions of the innovation eco-systems #1
D3.6.2 Dimensions of the innovation eco-systems #2
D3.6.3 Dimensions of the innovation eco-systems #3
T3.8 Overcoming organizational barriers against deployment
0%
D3.7 Technology exploitation strategies: overcoming organizational barriers
T4.1 Legal gaps and enablers for biorobotic devices and allied digital technologies
46%
T4.2 Governance Gaps: organizational challenges and standardization of service providers procedures
30%
T4.4 Open acceleration
43%
MISSION 3: NEXT GENERATION COMPONENTS
MANAGEMENT

2. PART I

This part presents the most relevant tools and strategies for assessing and monitoring over time the value and impact (economical and organizational sustainability, acceptability, ease of use) of robotic rehab solutions in the community of final users, healthcare professionals, patients and their families. These tools are usually adopted for:

- demonstrating that the proposed solutions are sustainable and can be reimbursed by the payers. Data reported in the dossiers that technology producers have to present for obtaining the reimbursability of the proposed healthcare solutions, and so increasing the adoption and diffusion of robotic health technologies into the market, are based on models and techniques reported in this deliverable;
- supporting potential adopters, such as healthcare providers, to evaluate whether the adoption and use of the developed and ready to the market robotic solutions produce economic and organizational benefits in their institution, given their organizational, economic and financial structure.

3. HTA- INTRODUCTION

As mentioned in Deliverables D3.2, HTA collects multidimensional, multidisciplinary, and multi stakeholder techniques and analysis for assessing the value of a health technology from different perspectives and interests. HTA covers dimensions related to the clinical, non-clinical, economic, organization, ease of use, acceptability, usability, willingness to adopt, to use, to pay, and the legal and ethical issues. The assessment of the mentioned dimensions guarantees that the proposed solutions are not only effective, not only cost- effective in the short run, but also sustainable over time.

3.1 WHY ROBOTS ARE NOT PILLS, AND THE ROLE OF HTA

At first glance, it may seem trivial to note that robots are not pills. However, there is a tendency to apply pharmacoeconomic principles and methods, originally defined and proposed for assessing the clinical and non-clinical impact and sustainability of pharmaceutical products, to medical devices and robots.This section highlights the differences between pills and robotic solutions in terms of costs, impacts, and the associated assessments.

Table 1 Differences between drugs and robotic solutions

Drugs	Robots
Principal action	
Pharmaco/Immunologic/Metabolic Chemical based	Mechanical, control, EEE, software…
Product Life Cycle	
Long life cycle Unchanging compound	…as medical devices, but younger... we still miss data/evidence
Clinical Evaluation	
Easy to blind	…no placebo
Usually, one end users	Multiple end users
Short learning curve	Long learning curve
Less dependent by settings/users	Strongly dependent by settings/users
Easy to standardize for RCT	Incremental innovation
	Complex to standardize
Use Issues	
Efficacy is less user-dependent	…as medical devices
Usually does not require training	Final user perception is crucial
Complications increase with use	
Diversity	
Mainly large multinationals	…as medical devices
Therapeutic	Extremely specialized SME and experts

Costs	
High overheads with quicker return	…not yet clear universal models (how to reimburse in public NHSs?)
Lower distribution costs	Extremely dependent upon local assets
No maintenance/installation	Maintenance costs

3.2 IMPLICATIONS FROM THE CLINICAL PERSPECTIVES

The primary distinction between robotics and pills is that pills entail standardized service delivery, whereas healthcare services incorporating robots are characterized by relatively high heterogeneity due to the heterogeneity of patients involved in rehabilitation.

As a result, the implementation of new solutions involving medical devices necessitates organizational changes, which are less pronounced compared to changes associated with drug therapy.

3.2.1 Implications for the industry

Robotic solutions and pills do not differ significantly in terms of R&D costs, as both require substantial investment. However, they do differ in marginal costs. While the marginal costs of producing a pill are relatively low, the same cannot be said for robotics. Consequently, industries face significant costs beyond the R&D phases, such as pilot studies and clinical trials. Therefore, achieving a sufficient sample size to demonstrate the effectiveness and cost-effectiveness of robotic solutions entails not only enrolment and follow-up costs but also high production expenses.

3.2.2 The need for a HTA approach

All the aforementioned differences between pills and robots highlight the necessity for a multidimensional, multistakeholder approach to assess the value of robotic rehabilitation solutions, extending beyond the clinical dimension. While the economic dimension is increasingly mandatory for drug assessments, factors such as organizational acceptability and the usability of robotic solutions are dimensions that cannot be overlooked when evaluating medical devices. In short, a HTA approach solicits to assess the value of health technology beyond the primary clinical endpoints.

3.3 SELECTION OF THE DIMENSIONS

In selecting dimensions of analysis, we adhere to a pragmatic approach rooted in Peirce's rule for clarifying ideas.

3.3.1 The Peirce's rule

Peirce's rule
Consider which effects, that might conceivably have practical bearings, we conceive the object of our conception to have. Then, our conception of these effects is the whole of our conception of the object.

Thus, the dimensions that characterize robotic rehabilitation comprise solely the practical consequences of robotic rehab. When selecting dimensions relevant to assessing robotic rehab solutions, we focus exclusively on practical consequences related to the adoption and diffusion of robotic rehab.

Peirce's rule also serves as a valuable tool for ex ante assessment of differences among dimensions and variables to be included in a Health Technology Assessment (HTA). If two dimensions that may seem similar yield different practical consequences, they should be treated as distinct. Conversely, if two apparently different dimensions result in the same expected practical consequence, they explain the same object.

The ex-post assessment of relationships between and within dimensions initially perceived as distinct adopting the Pericer rule, will be conducted through statistical analysis.

3.3.2 A top down versus a bottom-up approach

The consequences of adopting Peirce's rule are significant. It is evident that we prefer to begin with a reduced number of dimensions and variables, selected based on Peirce's rule, rather than collecting all possible dimensions and then deriving a reduced form through a bottom-up statistical approach. This approach is necessary since the units of analysis are patients, and gathering a vast amount of information directly from patients would impose too high an effort on them during the clinical trial. Needless to say, a bottom-up approach requires a large amount of complete data and an extensive list of questionnaires, which may discourage responses.

One might criticize the top-down approach in favor of a bottom-up pathway and reducing data complexity through less biased and more neutral statistical tools. However, a bottom-up approach is typically adopted in social science, where the objective is exploratory. In contrast, the aim of clinical and interventional studies is (or should be) clear and directed towards proving the non-inferiority of new solutions when compared with existing ones. This inherently implies that only a top-down approach can be accepted.

3.3.3 Selected dimensions for robotic rehab HTA

Consequences of robotic rehab solutions (and so dimensions of HTA) are related to the following dimensions:

- clinical issues;
- patients' and their families' quality of life and well-being (non-clinical dimensions) during and after the rehabilitation;
- acceptability and usability of the solutions;
- economic issues;
- different organizational and management challenges for service providers (organizations);
- different organizational and management challenges for service providers (healthcare professionals) with consequences on work related quality of life;
- ethical and legal issues related to (a) the clinical trials and HTA; (b) the tested solutions once they will be in the market.

3.4 IDENTIFICATION OF SCENARIOS

We adopted the following definition of scenario.

Adopted definition of scenario
A scenario is a system of interconnected solutions, stakeholders, and environments within which solutions operate through certain stakeholders and elements of the environment. These solutions are then applied to other stakeholders experiencing specific conditions.

The definition of scenarios is imperative in the case of HTA. They:

- Structure the cost and simulation models.
- Identify the challenges, risks, strengths, weaknesses, and limits of the proposed technologies.
- Shape the storytelling, which implicitly or explicitly guides the definition of market targets and business models.

From the perspective of technology, one should consider the relationship between robotic solutions, their applications, and the related environments as norms of reactions (refer to genetics and ethology). A norm of reaction describes genotypic forms in response to environmental factors. Indirectly, a norm of reaction explains why a specific genotype G1 is adapted to an environment E1 but not to E2. Similarly, scenarios for robotic rehabilitation describe how healthcare services change according to different conditions (such as those of the patient, hospital facilities, etc.). In Deliverable D3.1, we developed a general scenario accounting for the various rehabilitation regimes (inpatient, outpatient, at-home services) and patient conditions.

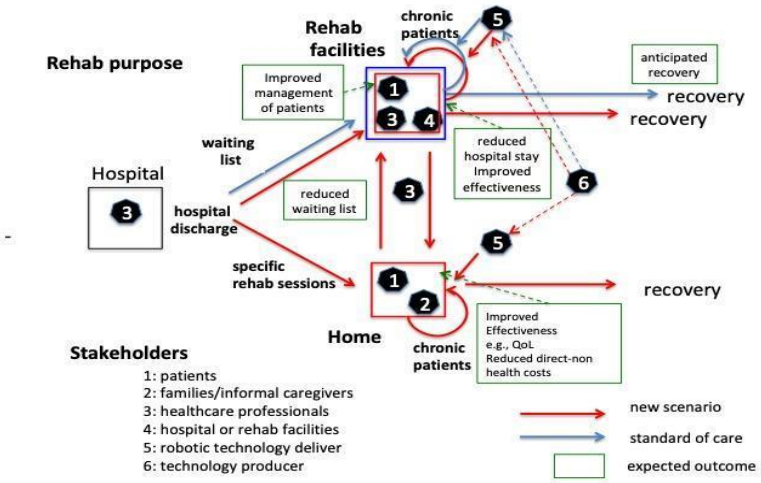


Fig. 1 The general scenario described in D3.1.

Fig. 1 presents a general new scenario of robotic rehabilitation. The proposed scenario also identifies the relevant stakeholders (see section 3.5). Scenarios for each specific disease (for instance, rehabilitation after stroke) will be designed within the definition of clinical protocols.

SELECTION OF THE VARIABLES

We provide certain criteria and principles for selecting variables to be used in assessing the value of robotic rehabilitation within Fit4MedRob.

3.4.1 General criteria for selecting variables

1. The dimensions that cannot be measured effectively are considered non-existent.

2. Additionally, if, for a particular dimension, the anticipated effort required to assess a specific robotic rehabilitation application using a particular tool exceeds the expected value of the gathered information, then that dimension should be measured using alternative and more cost-effective solutions, or alternatively, it should be bypassed.

3. We should prioritize quantitative and objective measures over impressions and qualitative approaches. However, there are certain dimensions and nuances that cannot be assessed quantitatively. This is particularly true when involving patients in describing their needs without imposing judgment or requiring closed answers. In such cases, open-ended questions are valuable complements to a quantitative approach. Additionally, conducting a quantitative text analysis based on word frequency (a sentimental analysis) can be highly beneficial.

3.4.2 Selected dimensions

For the identification, description and comments on the variables selected for the assessment of the value of robotic rehabilitation solutions, please refer to Deliverables 3.1 and 3.2.

3.5 SELECTION OF THE PERSPECTIVES - STAKEHOLDERS

The selection of stakeholder should be based on the definition of stakeholder.

Adopted definition of stakeholders
A stakeholder is a human being, a group of human beings, an institution or group of institutions that directly, or indirectly, transfer or receive value to and from robotic rehabilitation.

3.6 SELECTION OF THE LEVELS OF ANALYSIS

Two types of levels of analysis should be taken into account:

1) the level of analysis from a micro to a macro approach that involves the degree at which the units of analysis are aggregated from single agents to groups of agents, and the society;

2) the level of details of the analysis (especially considering the analysis of costs).

3.6.1 The level of analysis from the economic perspective

The levels of analysis are essentially three: micro, meso, and macro. To transition from a micro-perspective (focusing on disaggregated stakeholders such as final user behavior) to a meso-level (which involves singular organizations and groups), and finally to a macro scenario representing the aggregation of all micro behaviors, we require a condition of equilibrium known in economics as 'perfect competition'.

Naturally, the ability to derive macro-level behaviors from micro-level behaviors depends on the units of analysis: the type of stakeholder. For example, if the group of patients is considered, its behavior can be inferred as the sum of the behaviours of individual patients. This assumption relies on the premise that, despite the heterogeneity among patients, they do not significantly influence each other (excluding scenarios such as virus contagion). Conversely, the independence of behaviors is not guaranteed among service providers or technology producers.

3.6.2 The level of details in cost analysis

The level of details of the cost assessment depends on the type of technology that are compared. It is mandatory that the assessment of innovative technologies that are not part of a reimbursed service needs a micro-costing approach. For more details see Section 4.

4 THE ECONOMIC DIMENSION

4.1 TYPES OF ECONOMIC EVALUATIONS AND MEASURES OF ROBOTIC-REHAB COST-EFFECTIVENESS

In assessing the costs per unit of effect (sustainability) of robotic rehab solutions, and within the economic dimension of HTA, we will consider only comprehensive analyses. Comprehensive means that the analysis:

- will compare both costs and effects of the adoption and use of robotic rehab solutions;
- will compare costs and effects of alternative solutions and the standard of care.

The following table summarizes the principal comprehensive analyses for robotic rehab sustainability we will conduct in the next deliverables.

Table 2 Types of analysis and measures comparing costs and impact of robotic-rehab mixed solutions.

Type of analysis	**Variables and measured involving effects**	**Variables and measured involving costs**	**Summary measures (example on two alternatives)**	**Conditions**
Cost-minimization		- Direct health non-health costs, indirect costs - Cost from the perspective of hospital facilities	min (Cost A, Cost B)	Clinical studies will assess that traditional rehabilitation and mixed models of traditional rehab and robotic rehab have the same effectiveness
Cost-benefit analysis (**)	Willingness to pay (WTP) for an incremental improvement of health conditions (perspective of payers and hospital facilities)		CBR: cost benefit ratio: (Cost B - Cost A)/WTP	The adopted measures for assessing the impact of traditional and robotic-rehab solutions are too heterogeneous and the evaluation becomes too complex (*)
Cost-effectiveness analysis	Clinical and disease specific measures		ICER= (Cost B - Cost A)/(Eff. B - Eff. A)	
Cost-utility analysis	Generic measures such asquality of life		ICUR= (cost B - cost A)/(Utility B - Utility A)	
Sensitivity analysis (for each type of the above analyses)	The considered measures of effectiveness	The considered measured of costs	3-5 years total direct costs B - 3-5 years total direct cost A	
Budget impact analysis		Direct health costs		

(*) e.g, the exploratory statistics of the different measures of effectiveness is not able to significantly reduce data complexity.

(**) Beyond the necessity to manage data heterogeneity and complexity, the use of cost benefit-analysis and the assessment of the willingness to pay could be a good and efficient strategy for modelling pricing, reimbursements, and the related business models.

Table 2 provides an overview of the economic analyses that will be conducted on the technologies and conventional and new healthcare pathways identified and tested within Fit4MedRob.

4.2 TYPES OF ANALYSIS

The last columns of Table 2 summarize the rationale, scopes, and outcomes of the various analyses related to the economic dimensions of HTA. Here we offer more details on the considered analysis.

4.2.1 Cost-minimization

As described in the last column of Table 2, Cost-minimization analysis (CMA) is an economic evaluation used to compare the costs of different interventions or treatments when the outcomes are assumed to be equivalent. Unlike cost-effectiveness analysis (CEA) or cost-benefit analysis (CBA), which compare both costs and outcomes, CMA focuses solely on identifying the intervention with the lowest cost among alternatives that are considered equivalent in terms of outcomes. Cost-minimization analysis provides a useful framework for comparing the costs of different healthcare interventions when the outcomes are assumed to be equivalent. While it may not provide information on the value or cost-effectiveness of interventions, it can help healthcare providers and policymakers identify opportunities to achieve cost savings without compromising patient outcomes.

The analysis follows different steps:

1. Identification of Equivalent Interventions: to identify two or more interventions or treatments that are considered to be clinically equivalent in terms of efficacy, safety, and other relevant outcomes. These interventions may include different drugs, medical devices, surgical procedures, or healthcare delivery models.

2. Measurement of Costs. Once the equivalent interventions have been identified, to measure and quantify the costs associated with each intervention. Costs may include direct expenses such as drug costs, equipment costs, personnel costs, and overhead costs associated with the provision of healthcare services.

3. Comparison of Costs: The costs of the different interventions are compared to determine which intervention has the lowest cost.

4. Decision Making: The results of the cost-minimization analysis are used to inform decision-making regarding the selection of the most cost-effective intervention among those that are considered equivalent in terms of outcomes.

4.2.2 Cost-benefit analysis

Cost-benefit analysis (CBA) is a systematic approach to evaluating the costs and benefits associated with healthcare interventions, programs, or policies. It involves comparing the costs of implementing a particular healthcare intervention or policy with the benefits it generates, typically in monetary terms.

Cost-benefit analysis plays a crucial role in healthcare decision-making by providing a systematic framework for evaluating the economic efficiency of healthcare interventions and policies. It helps policymakers and healthcare providers allocate resources effectively to maximize the health benefits for the population within the constraints of limited budgets.

A CBA consists of the following steps:

1. Identifying the Intervention or Policy: The first step in conducting a cost-benefit analysis in healthcare is to identify the specific intervention, program, or policy being evaluated. This could range from the introduction of a new medical technology or treatment procedure to the implementation of a public health initiative.

2. Defining Costs and Benefits: Next, the costs and benefits associated with the intervention need to be identified and quantified. Costs may include direct expenses such as equipment, personnel, and operational costs, as well as indirect costs such as productivity losses. Benefits typically include improvements in health outcomes, such as reduced morbidity and mortality, as well as other societal benefits such as increased quality of life and productivity gains.

3. Measuring Costs and Benefits. Costs and benefits are quantified in monetary terms wherever possible. This involves estimating the dollar value of both the costs incurred by implementing the intervention and the benefits generated as a result. In healthcare, this may involve estimating the value of life years saved, avoided healthcare expenditures, and improvements in patient quality of life.

4. Discounting. Since costs and benefits may occur over different time periods, discounting is often applied to account for the time value of money. Future costs and benefits are discounted back to present value using an appropriate discount rate, typically reflecting the opportunity cost of capital.

5. Comparing Costs and Benefits. Once costs and benefits have been quantified and discounted, they are compared to determine whether the benefits outweigh the costs. This comparison is typically expressed as a cost-benefit ratio or net present value (NPV). A positive NPV indicates that the benefits exceed the costs, while a negative NPV suggests that the costs outweigh the benefits.

6. Sensitivity Analysis. Assessment of the robustness and reliability of the results through the following steps: selection of relevant variables, definition of a plausible range of values, adoption of those values in the model, comparison of results.

4.2.3 Cost-effectiveness analysis

Cost-effectiveness analysis (CEA) compares the costs and health outcomes of alternative interventions or treatments. It assesses the efficiency of healthcare interventions by examining the ratio of the incremental costs of an intervention to its incremental health benefits compared to a comparator, usually standard care.

CEA consists of the following steps:

1. Identification of Interventions. To identify the interventions or treatments being compared. These could include different drugs, medical devices, surgical procedures, healthcare programs, or policies. Measurement of Costs: Once the interventions have been identified, the costs associated with each intervention are measured and quantified. Costs may refer to drugs, medical equipment costs, personnel costs, direct non-health costs such as patient transportation, and indirect costs such as productivity losses.

2. Measurement of Health Outcomes. In addition to costs, the health outcomes associated with each intervention may include improvements in patient health status, such as reductions in symptoms, disease progression, morbidity, mortality, or improvements of disease specific quality of life.

3. As reported in Table 2.1, calculation of Incremental Cost-Effectiveness Ratio (ICER): The incremental cost-effectiveness ratio (ICER) is calculated by dividing the difference in costs between the interventions by the difference in health outcomes. The ICER represents the additional cost incurred to achieve one additional unit of health outcome compared to the alternative intervention.

4. Interpretation of results. Let consider the case in which we assessed the ratio between the difference in costs and effectiveness of the new solutions with respect to the old one as the standard of care.

A negative ICER may depend:

- on the fact that the difference in costs is negative and the difference in effectiveness is positive. This is the case in which the new solution is more effective than the old one and saves money. The new solution is cost-effective.

- on the fact that the difference in costs is positive and the difference in effectiveness is negative, the new solution is less effective than the old one and it is more expensive. Therefore, the new solution is not cost-effective.

A positive ICER may depend:

- on the fact that the both the difference in costs and effectiveness are negative. This is the case of a solution that is less effective but cheaper than the old solution. Since the first mandatory condition for a new health technology is to be, at least, non-inferior if compared with the standard of care, the new solution is not accepted for reimbursement.

- on the fact that the both the difference in costs and effectiveness are positive. This is the typical case of new incremental or radical health innovation. In this case ICER is compared with a willingness-to-pay (WTP) threshold, which represents the maximum amount that decision-makers are willing to pay for a unit of health outcome. If the ICER is below the WTP threshold, the intervention is considered cost-effective.

5. Sensitivity Analysis. Assessment of the robustness and reliability of the results through the following steps: selection of relevant variables, definition of a plausible range of values, adoption of those values in the model, comparison of results.

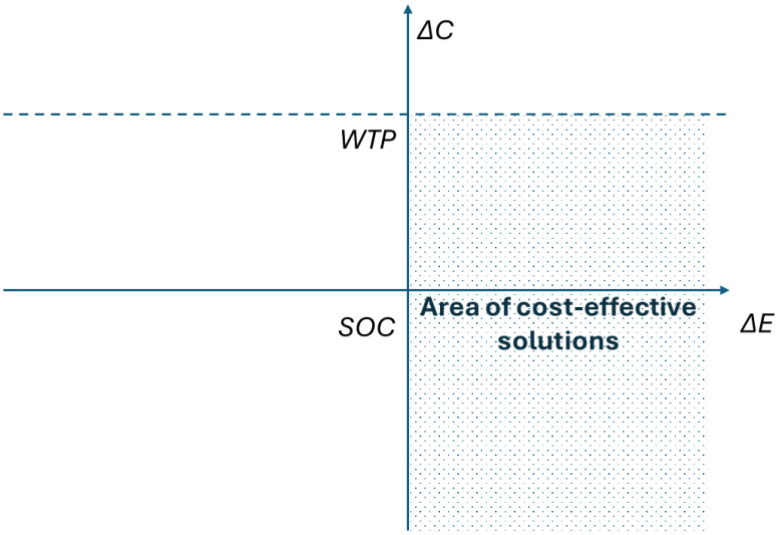


Fig. 2 Area of cost-effective solutions

4.2.4 Cost-utility analysis

Cost-utility analysis (CUA) evaluates the efficiency of healthcare interventions by measuring health outcomes in terms of utility, which is a measure of overall well-being or quality of life, and comparing the costs incurred to achieve these outcomes.

1. Identification of Interventions.
2. Measurement of Costs.
3. Measurement of Health Outcomes. Health outcomes are typically measured in terms of utility, which represents the individual's overall well-being or quality of life expressed in terms of utility. Utilities are often assessed using standardized preference-based measures such as the EuroQol Five-Dimension (EQ-5D) questionnaire or the Health Utilities Index (HUI). At each health condition identified through the generic questionnaires on quality of life are associated country-specific utility scores. Usually, there are already published studies that report how to transform combinations of health conditions into [0-1] utility scores based on techniques such as the Standard Gable and the Time Trade off approaches. In the case of the Standard Gable, the utility of condition i corresponds to the probability p that makes indifferent a patient to remain in i or to accept the intervention that gives him the best health condition with probability p and the worst health condition (usually the death) with probability 1-p. The Time Trade off approach identifies the utility of a health condition i as the ratio between the number of expected years in good well-being X that make indifferent the patient compared with the expected life years EL(i)> X corresponding to its current health condition i: u(i)=X/EL(i).
4. Calculation of Quality-Adjusted Life Years (QALYs). QALYs are calculated by multiplying the time spent in each health state by the utility associated with that health state. For example, if an individual spends 5 years in perfect health (utility = 1) and 12 years in a health state with a utility of 0.25 equal 5*1+12*0.25=8 QALYs.
5. Calculation of the Incremental Cost-Utility Ratio (ICUR) as the ratio between differences in costs and differences in QALY.
6. Sensitivity Analysis. Assessment of the robustness and reliability of the results through the following steps: selection of relevant variables, definition of a plausible range of values, adoption of those values in the model, comparison of results.

4.2.5 Budget impact analysis

Budget Impact Analysis (BIA) is a type of economic evaluation used to assess the financial impact of adopting a new healthcare intervention or technology within a specific budgetary context.

BIA provides decision-makers with valuable information about the financial implications of adopting robotic rehab solutions. The BIA consists of the following steps.

1. Identification of the Intervention: to identify the new healthcare intervention or technology being considered for adoption. This could include new drugs, medical devices, diagnostic tests, treatment protocols, or healthcare programs.

2. Assessment of Current Budgetary Status: to assess the current budgetary status of the healthcare system or organization in which, considering, for instance, Fit4MedRob, the robotic rehab solution will be implemented. This involves identifying the sources of funding, such as government budgets, insurance reimbursements, or out-of-pocket payments, and determining the available financial resources (a BIA traditionally assesses costs on the perspective of the payer (e.g, the national or regional healthcare system, the insurer, etc.).

3. Estimation of Costs: Once the intervention and budgetary context have been identified, the costs associated with adopting and implementing the intervention are estimated. This includes both direct costs, such as the cost of the intervention itself, as well as indirect costs such as training, administration, monitoring, and infrastructure upgrades.

4. Projection of Budget Impact: Using available data and assumptions, the budget impact is projected over a specific time horizon, typically 3-5 years of market uptake. This involves estimating: -

a. the incremental costs incurred as a result of adopting the intervention and comparing them to the baseline or status quo scenario where the intervention is not adopted.

b. the market uptake of the technologies and the degree of replacement and integration with the current healthcare services and technologies.

5. Sensitivity Analysis.

6. Interpretation of Results: The results of the budget impact analysis are easy to interpret. A negative difference in costs between the new and the current scenario implies that the new solutions save money.

7. Implementation plans and strategies to manage the budgetary implications of adopting the new solutions (the robotic rehab solutions), reallocations, negotiations with payers or suppliers, reimbursement adjustments, or other financial arrangements.

4.2.6 Sensitivity analysis

Sensitivity analysis is conducted to assess the robustness of the results to changes in key assumptions or parameters of the models. It may be carried on considering a deterministic (Deterministic sensitivity analysis, DSA) versus a probabilistic approach (probabilistic sensitivity analysis, PSA). Both approaches are valuable tools for evaluating the robustness of economic evaluations and informing decision-making in healthcare. However, they differ on:

1. the nature of Analysis: DSA is conducted varying one input parameter at a time while holding all other parameters constant. This allows for the examination of how changes in specific parameters impact the results of the economic evaluation. PSA involves simultaneously varying multiple input parameters across probability distributions. This approach captures the joint uncertainty in multiple parameters and provides a more comprehensive assessment of overall uncertainty.

2. Handling Uncertainty: DSA provides insights into the impact of deterministic changes in input parameters on the study results. It does not explicitly quantify the uncertainty associated with each parameter but rather examines the effects of varying individual parameters. PSA explicitly incorporates uncertainty by sampling from probability distributions for each input parameter. By simulating multiple iterations of the model using randomly sampled values for all uncertain parameters, PSA generates a distribution of outcomes, allowing for the estimation of confidence intervals and probability distributions around key study results.

3. Output. While DSA typically provides point estimates or ranges of outcomes for specific scenarios, PSA produces probability distributions or confidence intervals of the measures that summarized the analyses described in Table 1.

4. Interpretation: DSA identifies which parameters have the greatest influence on the results. SA allows decision-makers to assess the overall uncertainty.

All the results of the mentioned analyses inform decision-making regarding the selection of the most cost-effective solution. For more details see Drummond et al.2005; Briggs et al. 2006; Gray et al. 2010.

4.3 TYPES OF COSTS

The following families of costs must be considered:

- direct healthcare costs limited to rehabilitation regimes (inpatient, outpatient and at home), robotic technologies (consumables, energy, maintenance costs) personnel directly involved in rehabilitative sessions and the related initial training.
- direct non-health costs: traveling costs, out-of-pocket costs, etc.
- indirect costs: productivity loss of the patient and his/her informal caregiver.

For more details see section 4.4.2.

4.4 DESIGN OF COST MODELS FOR REHAB ROBOTICS: PRINCIPLES AND STRATEGIES

In this section we try to develop some principles that should guide the design of a general cost model for assessing the economic impact and sustainability of robotic rehab solutions. Following the principles, we also offer a basic and general model of costs that can be tailored for different and new specific robotic solutions.

4.4.1 Principles for a model of robotic-rehab costs

1. The model should be flexible to:

    a. Consider different regimes of rehabilitation, such as inpatient, outpatient, and at-home settings.

    b. Account for the diverse impacts of robotic solutions.

The model should also:

2. Adopt a multistakeholder approach: for each selected stakeholder, we should compare costs and revenues. The sustainability of robotic rehabilitation depends on ensuring that the costs (both tangible and intangible) are lower than the revenues (both tangible and intangible) for each involved stakeholder.

Therefore, for each type of selected stakeholder the model should consider:

- costs related to the followed type of rehabilitation.
- effectiveness of that type of rehabilitation.
- other measures corresponding to the dimensions selected by the HTA approach such as organizational key performance indicators (KPIs) (bed turnover, etc.) are mandatory for assessing the impact of novel solutions from the hospital facility. From the perspective of final users such as patients, organizational implications are mandatory only if the rehabilitation service is delivered at home and other indicators are more relevant.

3. Employ a micro-costing approach. Since there is no established reimbursement standard for new solutions, and new robotic solutions should be evaluated based on their real costs, considering:

    a. Technology-related costs.

    b. Personnel-related costs.

4. Recognize the specificity of complementary robotic solutions. The cost model should compare alternative rehabilitation models rather than individual technological alternatives. Robotic rehabilitation represents a blend of various robotic technologies.

5. Acknowledge that robotic solutions are meant to support, not replace, healthcare professionals. Therefore, the model should compare rehabilitation models rather than individual robotic solutions. The comparator, standard of care, integrates different and complementary robotic solutions.

6. Consider that not all patients eligible for standard rehabilitation are suitable for robotic solutions, and not all rehabilitation centers can exclusively provide robotic solutions: the new rehabilitation solution should be a hybrid model where each rehabilitation center decides the percentage of sessions delivered using robotic solutions.

7. Rehabilitation sessions are the units of analysis.

4.4.2 The general model

The general model (the perspective of the society) consists of three interconnected submodels, each representing a type of involved stakeholder: A. the patient and their families, B. the hospital facility, and C. the payer, such as the Regional Healthcare System, D: Healthcare professionals; E. the society.

Traditional models often consider only stakeholders A and C, or solely C, or E (without considering the perspective of the hospital facility). Consequently, we assess the impact of a new solution from the perspectives of the payer, patients, and society, including indirect costs (productivity loss), while overlooking the economic reasons why a reimbursable solution may be unsustainable for hospital facilities.

Structure of the model

The multistakeholder model is structured as follows.

Hospital facility

Costs

1. Each hospital facility delivers to n patients per year a number of s sections per patient. A regime of rehabilitation consists of three percentages p1+p2+p3=1 corresponding to the percentage of s that are inpatient, outpatient, and at home. The percentages are fixed according to:
   - the hospital facility structures;
   - the severity of patients' conditions;
   - the use of mixed solutions including robotic rehab.
2. Each rehabilitation section is structured in terms of:
   - duration (D);
   - personnel involved physiotherapists, Health Care Assistant (HCA, in Italian OSS), and for each type of personnel involved:
     - time spent in the rehab session;
     - the number of involved types;
     - the hourly wage;
     - hours of initial training with the new technology;
   - technologies involved.
3. For each technology involved in each rehabilitation section:
   - original cost and cost related annual maintenance costs;
   - life cycle (years);
   - costs of associated with consumables;
   - Costs associated with energy power.

The total cost models associated with conventional (RC) and robotic rehab (RR) in a given hospital facility per session and per person will be the following.

$$CRC_r = nx_{CRRr} S_r \; R_{phr} W_{phr} \;\; TS_{ph} * (1 + \frac{x_{CRr}}{n} ind_r) \quad (1)$$

$$CRR_r = nx_{RRr} S_r \; (R_{phr} W_{phr} \; \frac{TS_{ph}}{nt_{phr}} + R_{ha} W_{har} \;\; \frac{TS_{ha}}{nt_{har}} + \frac{PTr(1+mtr)}{nx_{RRr} S_r lf_{Tr}} + et_r + ct_r \;\;)(1 + \frac{x_{RRr}}{n} ind_r) \quad (2)$$

Where:

- n is the number of patients early assisted or managed by a specific hospital facility. It is assumed that for outpatient and at home scenarios a rehabilitative structure is always involved (it may deliver a tele-rehabilitation service).

- xRRr and xCRRr are the percentage of total patients assisted with conventional and robotic solutions in the rehab regime r. Where *r* can assume letters I, O, H, according to impatient, outpatient, and at home rehabilitation, respectively.

- S_r is the per patient total number of rehabilitation sessions in regime *r.*

- R_{phr} and R_{har} are the number of physiotherapists and healthcare assistants involved in each session and for different rehabilitation regimes. For instance, R_{haH} where H means at home rehabilitation could be zero.

- W_{phr} and W_{har} are the hourly salary of physiotherapists and healthcare assistant (OSS in Italy) if they are involved in rehab scenario r;

- TS_{ph} and TS_{ha} are the time (expressed in hours) spent by physiotherapists and healthcare assistants for each session and per patient. It is assumed that this parameter does not change in different rehab scenarios;

- nt_{phr}, nt_{har} are the number of patients that each physiotherapist and health care assistant can contemporarirly manage during a rehab session of type r.

- PTr is the original price of the technology or the set of technologies adopted for rehabilitation of type *r*;

- mtr is the annual maintenance cost of the robotic technology involved in type r *rehabilitation* as a percentage of the technology original price. This price is divided by total number of annual sessions and the life cycle of the involved technologies in the different regimes.

- et_r, ct_r are the energy costs and cost of consumables per session and type or technology involved in the rehabilitation regime r.

- ind_r indicates indirect costs as the percentage of the directed costs associated with rehabilitation sessions and compatible with a rehab regime *r.* For instance, it is expected that $ind_H = 0$.

Table 3 Different cost models for types of rehabilitation (conventional vs robotics) and rehabilitation regimes

	Inpatient	**Outpatient**	**At home**
Conventional rehab	Equation (1) and r=I	Equation (1) and r=O	Equation (1) and r=h
Robotic rehab	Equation (2) and r=I	Equation (2) and r=O	Equation (2) and r=h

Alternative healthcare pathways may be designed and compared considering a combination of different regimes. Therefore, the general models of costs can be tailored as the sum of different combinations of costs reported in Table 3, and considering the number of programmed rehab sessions.

Outcome (per type of pathway)

Outcomes refer to specific rehabilitation pathways consisting of a defined order of types (inpatient, outpatient, at home, and conventional and robotic) and number of sessions. Outcomes are clinical, non-clinical, organizational KPIs defined and selected in Deliverables D3.1 and D3.2.

Health economic dimensions

The ratios between differences in costs and outcomes of the alternative rehab regimes and technologies will allow the assessment of incremental cost-effectivenesses (ICERs) of alternative solutions. The society collects the perspective of hospital facilities, patients, payers, also assessing the impact of alternative rehab regimes and technologies on restoring working productivity (reducing indirect costs).

4.4.3 Economic and organizational “income statement” for each involved stakeholder

4.4.3.1 Hospital facility

The “income statement” of each hospital facility consists of different sessions able to:

- compare revenues and reimbursement, and costs that are useful information for assessing the sustainability of the current and/or future robotic rehab solutions implemented in that centre;

- assess the clinical, non-clinical and organizational outcome of patients' pathways (conventional and robotic rehab);

- assess and compare the cost-effectiveness of the alternative pathways.

A first session assesses the reimbursement and revenues of the specific centre in delivering rehabilitation.

Table 4 Hospital facility's statement. Characteristics of rehab services delivered.

Centre ID		Period		From		To	
		number of sessions					
		Conventional			Robotic		
		Inpatient	Outpatient	At home	Inpatient	Outpatient	At home
	% reimbursed by third payers						
	% directly paid by the final user						
Revenues							
Revenues	per session reimbursement						
	per session revenues						
TOTAL REVENUES							**0**

A second session assesses the related costs considering personnel, technology, and indirect costs.

The difference between total revenues and total costs is the total gross profit of the rehabilitation activity for each specific centre.

Table 5 Hospital facility's statement - costs.

Costs								
Personnel								
Physiotherapist	Number involved per session							
	Time spent per session (h)							
	# pzt anaged simultaneously							
	Operator training (h)							
	Hourly salary							
	Per session cost							
Healthcare assistant	Number involved per session							
	Time spent per session (h)							
	# pzt anaged simultaneously							
	Operator training (h)							
	Hourly salary							
	Per session cost							
Per session total personnel costs								0
Technology (for each involved technology)								
Technology 1	Price							
	Life cycle							
	Maintenance annual costs							
	Energy power							
	Consumables							
	Per session cost							
Technology n	Price							
	Life cycle							
	Maintenance annual costs							
	Energy power							
	Consumables							
	Per session cost							
Per session total cost technology		0	0	0	0	0	0	0
Indirect costs (%)								
TOTAL costs								
PROFITS								0

A third session collects the clinical, non-clinical outcomes of alternative healthcare pathways (represented as the number of sessions for each type of rehabilitation and the order of types) and, considering the obtained costs, the different ICERs.

Table 6 Hospital facility's statement. Cost-effectiveness of alternative healthcare pathways.

Cost-effectiveness							
Conventional							
Dimension 1				Dimension n			
HP2	**....**	**HPn**			**HP2**	**....**	**HPn**
				HPn+1			
				HPn+2			
				HPn+k-1			
Involving robotic solutions							
Dimension 1				Dimension n			
HP2	**....**	**HPn**			**HP2**	**....**	**HPn**
				HPn+1			
				HPn+2			
				HPn+k-1			
	...						

[HP: Healthcare Pathway]

The last session compares the organizational KPIs (selected among the dimensions defined in Deliverable D3.2) of alternative pathways.

Table 7 Hospital facility's statement.
Performance assessment through organizational KPIs.

Organizaitonal KPIs					
		HP1	**HP2**	**....**	**HPn**
Organizatoinal KPIs	Number of dedicated beds				
	Length of hospital rehabilitation				
	Patient waiting time				
	Number of beds				
	# annual resignations				
	Turn over beds				
	# readmission				
	Rate of readmissions				
	Bed occupancy rate				
	Overall surface area				
	Dedicated surface				
	% of facility occupancy				

4.4.3.2 The patient and his/her family

Patients and their families compare their monthly income with the out-of pocket costs and % of reimbursement.

In their statement there are also the non-clinical outcomes that are also reported, as average, in the hospital facility data where the patient follows the rehabilitation sessions.

Also, the family statement reports the direct non-health costs such as traveling costs, leisure time of the relatives that assist the patient in their leisure time.

The dedicated document consists of the following sections:

1. Personal characteristics.
2. Types or rehabilitation.
3. Outcomes.
4. Costs related to the rehabilitation phase.

Table 8 The patient's statement.

Patient ID (anonymized)		Centre		From		to
Personal characteristics						
	v1	...				vn
Rehabilitation characteristics						
Date of the first visit						
Date of the first rehab session						
			Number of programmed sessions			
		Conventional			Robotic	
	Inpatient	Outpatient	At home	Inpatient	Outpatient	At home
	1	2	3	4	5	6
Number of programmed sessions						
Number of completed sessions						
Order of session						
Otucome						
	Measure 1	Measure 2	...	Measure n	Acceptability	Usability
Non-clinical outcome						
Costs						
Direct health care costs	**Amount**	**% reimbursed**				
Purchase of prescription drugs						
Purchase of drugs at a pharmacy without a prescription						
Medical tests or examinations performed during or after consultations						
Expenses for the purchase of medical devices						
Other paramedical treatment or care						
TOT. Direct health costs						
Direct non-medical costs						
Travel expenses for visits or rehabilitation sessions						
Average distance from your home to the rehabilitation center (km)						
Parking expenses						
Lodging expenses to travel to visits						
Expenses for specialist visits						
Home renovations to meet the patient's needs						
Time spent by a formal caregiver to assist the patient at home						
The hourly wage of the formal caregiver or companions other than parents						
The amount of free time of the informal (family) caregiver to assist the patient						
Other expenses						
TOT. Direct non-health costs						
Indirect costs (lost productivity)						
The average daily wage of informal caregivers (parents and other family members)						
The total work days lost by the patient						
The total work days lost by the informal caregiver						
TOT. Costs						

4.4.3.3 The payer

The payer's statement collects data on the sessions reimbursed (direct health costs) to all the centres involved in rehabilitation and the average of clinical and non-clinical outcomes taken among the different centres.

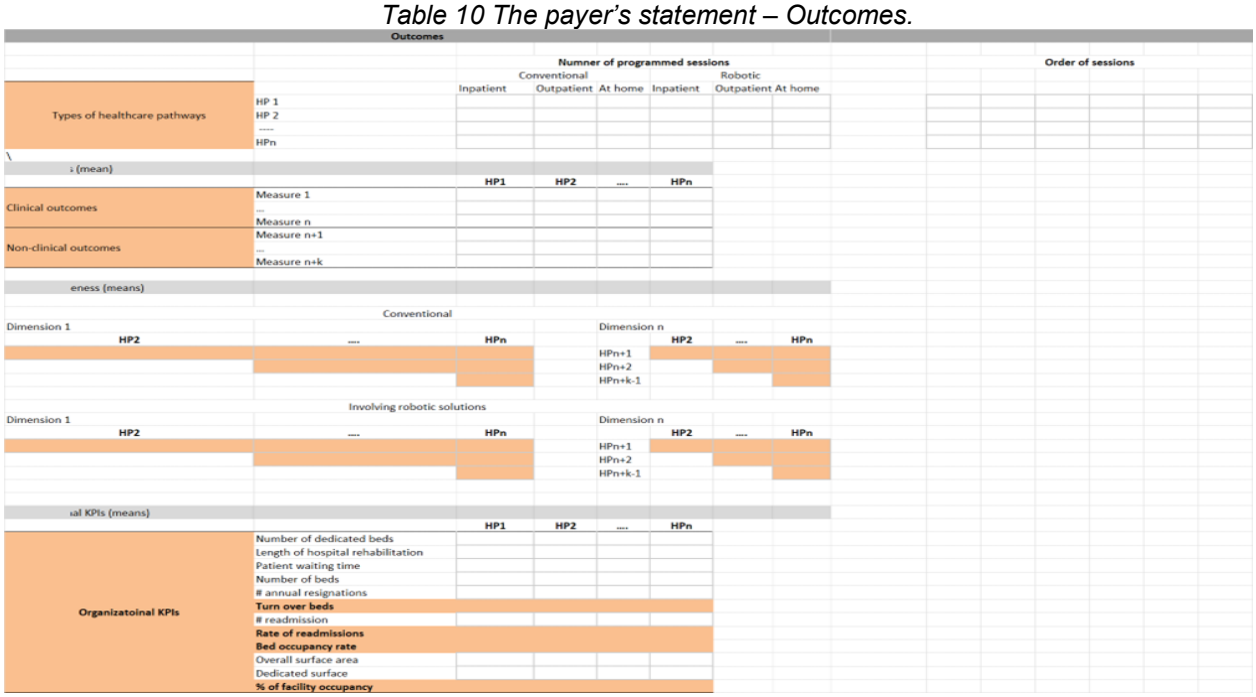
Since in the Italian scenario the payer is (in the majority of cases) also the decision-maker that, according to the comparison of costs and outcomes, decides to reimburse the new services, the general statement of the payer also collects data of outcomes coming from the different involved hospital facilities. A first section collects the total reimbursed services that are a cost for the payer.

Table 9 The payer's statement- costs.

		Period	From		To			
		Costs						
Direcet health costs		Number of total sessions						
Hospitalization and rehab related costs		Centre 1	Centre 2	...	...	....	Centre n	Per session reimbursement
Conventional	Inpatient							
	Outpatient							
	At home							
Robotical	Inpatient							
	Outpatient							
	At home							
	TOTAL REIMBURSD							TOT
Therapies								
Other direct health costs								

A second section collects and summarizes the mean of the observed outcomes and cost-effectiveness of the same services each hospital facility experienced.

Table 10 The payer's statement – Outcomes.



4.4.3.4 The healthcare professional

The statement of the healthcare professional consists of two sessions related to his/her experience on the different types of rehabilitation and the outcomes related to his/her activity.

Table 11 The healthcare professional's statement.

Patient ID (anonymized)	Centre		From		to	
Professional characteristics						
	v1	...				vn
Activity						
	Number of assisted sections					
	Conventional			Robotic		
	Inpatient	Outpatien	At home (remotly)	Inpatient	Outpatien	At home (remotly)
Number of patients						
Number of sessions						
Outcome						
Acceptability						
Usability						
Quality of life related to work						
....						

4.4.3.5 The society

The society's perspective sums the different perspectives: outcomes and costs of all conventional and robotic rehab services from the perspective of the selected stakeholders.

4.4.4 The relationships between costs and revenues among the different stakeholders

It is evident that revenues generated by hospital facilities through reimbursements, as well as the costs covered for reimbursed patients, are considered expenses from the perspective of the payer. The payer can decrease these costs

by reducing coverage for patient expenses. However, reducing public health expenditures leads to a decrease in citizens' income, resulting in negative consequences for the quality and accessibility of healthcare services in the medium and long term (with an increasing of long run costs).

4.5 SIMULATION TOOLS: PRINCIPLES, PERSPECTIVES AND ADOPTION IN THE PROJECT

4.5.1 Markov Models

A Markov model is a time process that satisfies the Markov property.

Let consider the case in which the time process X_t describes the evolution of a specific disease over time. So that at time t=0 the health conditions of a patient are denoted by, x_0 , …, at time t=n the health conditions of the patient are x_n .

x may correspond to levels of clinical and non-clinical measures that summarize the disease progression.

One may try to forecast disease progression by identifying the following conditional probability:

given that at time t=0 the health conditions were x_0 , at time t=1, x_1 , at time t=n-1, x_{n-1} , what is the probability that at time t=n the disease progression is at a level x_n ?

p($X_n = x_n | X_0 = x_0, X_1 = x_1, \cdots X_{n-1} = x_{n-1}$) .

If:

p($X_n = x_n | X_0 = x_0, X_1 = x_1, \cdots, X_{n-1} = x_{n-1}$) $= p(X_n = x_n | X_{n-1} = x_{n-1})$

then the process X_t satisfies the Markov property. $p(X_n = x_n | X_{n-1} = x_{n-1})$ denotes the transition probability (TP). If TPs do not depend on time, then X_t is a time homogeneous Markov process. To summarize, the Markov model describes a process in which the probability of being n a health condition X_n at time n depends on the health conditions at time n-1 only.

Markov models could be relatively simple and powerful solutions for assessing the medium and long-run impact of mixed models of robotic rehabilitation.

Stroke Rehabilitation

A study published in the journal Stroke in 2004 titled "A Markov model for evaluating cost-effectiveness of stroke units" by Heuschmann et al. developed a Markov model to assess the cost-effectiveness of stroke units compared to conventional care in stroke rehabilitation. The model evaluated transitions between different health states (independent living, nursing care, etc.) over time and incorporated data on costs and outcomes from clinical trials and observational studies.

Cardiac Rehabilitation

In the context of cardiac rehabilitation, a study published in the Journal of the American College of Cardiology in 2012 titled "A Markov Model of the Cost-Effectiveness of Patient Navigation Programs for Cardiovascular Disease Risk Reduction in the United States" by Moran et al. utilized a Markov model to evaluate the cost-effectiveness of patient navigation programs for cardiovascular disease risk reduction. The model simulated transitions between different health states (cardiovascular events, health behaviours, etc.) and incorporated data on costs, health outcomes, and program effectiveness.

Orthopedic Rehabilitation

A study published in Value in Health in 2019 titled "A Cost-Effectiveness Model of a Multidisciplinary Strategy to Treat Patients with Chronic Low Back Pain in the United States" by Assi et al. developed a Markov model to assess the cost-effectiveness of a multidisciplinary strategy for treating patients with chronic low back pain. The model simulated

transitions between different treatment pathways (physical therapy, medication, surgery, etc.) and health states (pain relief, functional improvement, etc.) over time, incorporating data on costs, health outcomes, and patient preferences.

Pediatric Rehabilitation

Another example is a study published in the Journal of Pediatric Rehabilitation Medicine in 2021 titled "Cost-effectiveness of telerehabilitation in pre-school children with developmental disabilities in China: a Markov model analysis" by Tang et al. This study developed a Markov model to evaluate the cost-effectiveness of telerehabilitation compared to conventional rehabilitation for preschool children with developmental disabilities in China. The model simulated transitions between different developmental outcomes and incorporated data on costs, health outcomes, and program effectiveness.
These examples demonstrate how Markov models have been applied to evaluate the cost-effectiveness and outcomes of rehabilitation interventions across different clinical populations and settings.

Principles and a general Markov-model relevant in Fit4MedRob.

In applying the Markov models for forecasting the medium and long-time sustainability of robotic rehab solutions we will adopt the following principles and methods.

1. We need to differentiate between two types of rehabilitation scenarios:
   a. those requiring periods of rehabilitation over time, and
   b. those necessitating rehabilitation for a fixed duration, occurring only once.

2. In scenario (b), we will instead employ time-dependent Markov Models (Tattar and Vaman, 2014; Bakoyannis et al., 2019), tailored to the specific disease types and corresponding rehabilitation regimens outlined in Figure 1.3.

We also assume that:

1. The choice of rehabilitation regimen is contingent upon the severity of the disease and the patient's health status.

2 While the typical time unit for Markov models is a month or a year, in our context, we will utilize the number of rehabilitation sessions.

3. Transition probabilities will be derived from transition rates observed during clinical trials. The Markov model will integrate predefined care pathways (ex-ante) and deviations justified by the real conditions of patients (ex post). While traditional Markov models applied to rehabilitation usually model disease progression, the new proposed Markov model integrates the interplay of specific care pathways and disease progression.

4. Regarding point 3, if the rehabilitation regimen is predetermined (ex-ante), transition probabilities will be calculated as the ratio between the total number of completed rehabilitation sessions and the number of sessions indicating a switch in the rehabilitation regimen. For instance, let consider a care pathway where 40 rehabilitation sessions are scheduled, with the last 10 sessions transitioning to an at-home regimen through tele-rehabilitation if the patient meets predefined targets. If a patient has completed 30 sessions under an inpatient regimen, the probability of transitioning to an at-home regimen would be 1 minus the difference between the expected and actual health conditions (E(HC) - (HC)). The probability of remaining in an inpatient condition would be close to 0, plus E(HC) - (HC). The percentage of missed transitions, representing deviations from the expected care pathway, as a function of E(HC) - (HC), can be observed during clinical trials and incorporated into the Markov Model.

5. Costs and effects such as quality of life in each rehab regime will be assessed following principles expressed in sections 4.1-4.3.

6. Simulation will consider an initial cohort of 1,000 patients in an inpatient rehabilitation regime.

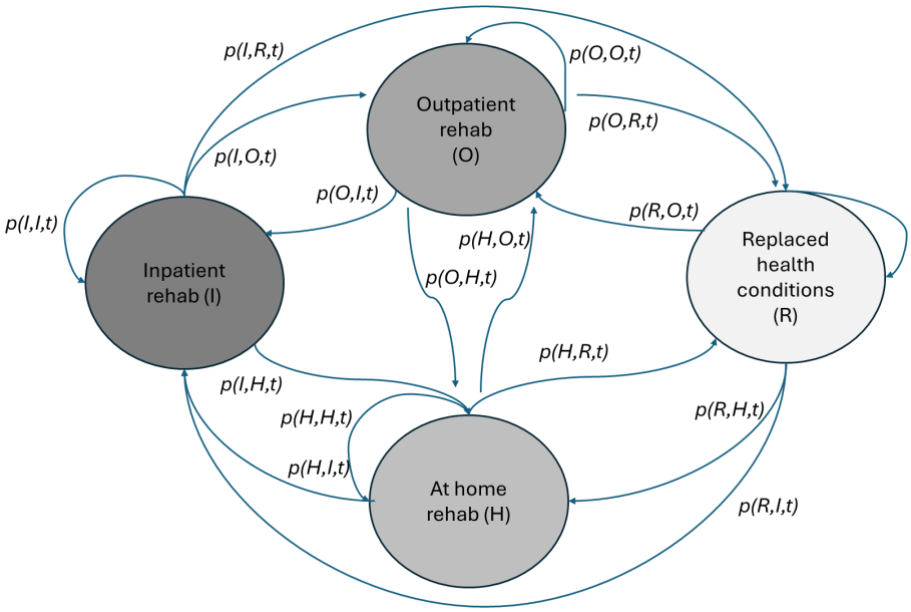


Fig. 3 The general Markov model adopted in Fit4MedRob.

Model of Figure 3 is a non-homogeneous Markov model consisting of four states and 16 transition probabilities.
As certain care pathways may not account for specific rehabilitation regimens or direct transitions between two or more regimens, some transition probabilities depicted in Figure 3 may be zero. Consequently, the general Markov model illustrated in Figure 3 can not only facilitate comparisons between various technological solutions within the same care pathways but also evaluate the same technology across different healthcare pathways, as well as different technologies across various healthcare pathways.
Differences among pathways that integrate robotic rehabilitation solutions may vary in:

1. The types of rehabilitation.
2. The probability of replacing health conditions after a given number of rehab sessions.
3. The costs associated with each rehabilitation regimen.
4. The probability of transitioning from one rehab regimen to another.

An example:

Let consider the case of after stroke rehabilitation where traditional versus robotic-rehab solutions are compared.

Conventional rehabilitation (CMM model)

In a conventional rehabilitation pathway, the “at home rehab” is not contemplated. The related clinical trial has been designed considering:

Rehabilitation care pathway

A rehabilitation session for conditions that need inpatient visits consists of S sessions.

After S inpatient sessions one may follow additional So outpatient rehab sessions, if his or her health conditions meet a threshold t1 obtained through disease specific and or generic measures. After the inpatient regime, according to a threshold t2, the patient is declared restored, or he/she needs another period Sp of programmed inpatient rehabilitation.

Costs

Inpatient costs are ic and outpatient costs *oc*, per session.

Direct non-health costs are *dnc per sessions (e.g, they are zero in case of inpatient and dnc* in case of outpatient rehab such as traveling costs.

Indirect costs correspond to one day (1) lost in inpatient rehab and *icp* days in outpatient rehab. The daily salary of a patient is *w1* and of his or her informal caregiver *w2.* The informal caregiver loses *hh* hours a day for accompanying the patient at the rehabilitation centre.

Effectiveness

1) A patient in an inpatient and outpatient rehab regime has quality of life scores of *qi* and *q0*, respectively. Let *qr* be the quality of life for restored patients. Without loss of generality, we assume that qi<qO<qr.

2) Transitions:

   a) a patient that follows an inpatient rehab has the following probability to pass to another regime:

   $p(I,0,t) = 1$ if t=S and x(t)=q0

   $p(I,0,t) = 0$ otherwise

   p(I, R) = 0

   $p(I,I,t) = 1 - p(I,0,t)$

   where x(t) is the vector of parameters clinicians assume for monitoring health conditions.

   b) the probability to pass from a outpatient regime O to the states R, and I are given by:

   $p(O,R,t) = 1$ If t=S+So and x(t)=qr

   $p(O,R,t) = 0$ otherwise

   $p(O,I,t) =$ 1 if x(t) < q0

   $p(O,I,t) = 0$ otherwise

   $p(O,O,t) = 1 - p(O,R,t) - p(O,I,t)$.

   The Markov model for conventional rehabilitation is represented in Figure 4.

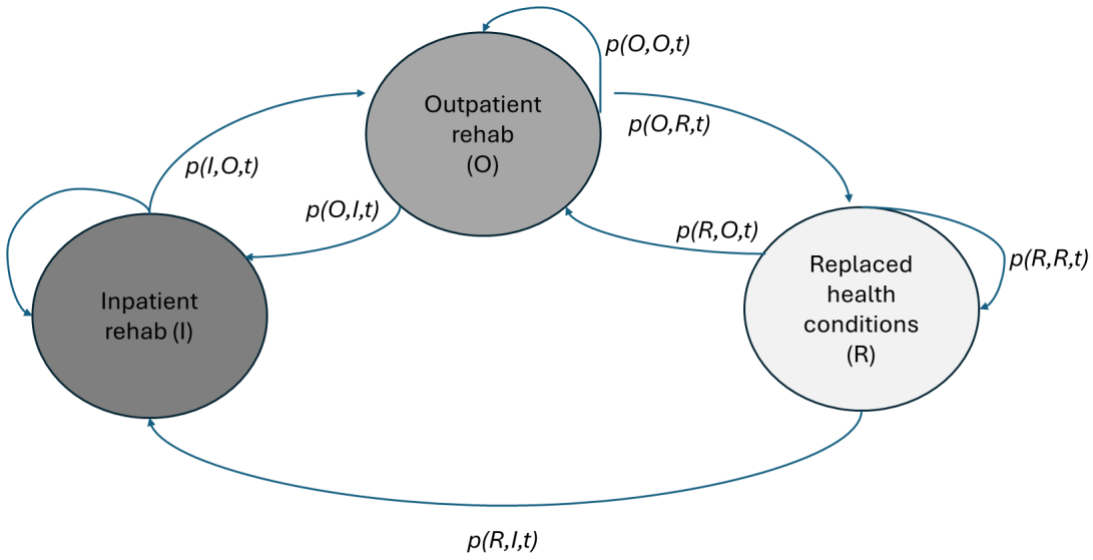


Fig. 4 Markov model of conventional rehabilitation.

New rehabilitation pathways including robotic rehab solutions (NMM model)

1. Rehabilitation care pathway
   a. A Rehabilitation session for conditions that need inpatient visits consists of S1 sessions.
   b. After S1 inpatient sessions one may follow additional So1 sections in outpatient regime, or Sh sessions at home, if his or her health conditions meet a threshold *t1'* or *th* obtained through disease specific measures. After the inpatient regime, according to a threshold, the patient is declared restored or he/she needs another period Sp of programmed inpatient rehabilitation, at home or inpatient.
2. Costs

a. The costs of inpatient and outpatient rehabilitation differ from traditional rehabilitation because of the introduction of robotic technologies. Direct health costs are *ci', co', ch* for inpatient, outpatient and at home robotic rehab, respectively.
b. Direct non-health costs are *dnci per session (e.g,* they are close to zero in case of inpatient and *dnco* and *dnch* in case of outpatient and at home rehab).
c. Indirect costs correspond to one day (1) lost in inpatient rehab, *ico* days in outpatient rehab and *ich* in tele-rehabilitation per session. The daily salary of a patient is *w1* and of his or her informal caregiver *w2.* The informal caregiver loses *hh'* for accompanying the patient at the rehabilitation centre and *hr'*.

3. Effectiveness
   a. A patient in an inpatient, outpatient and tele rehab regime has quality of life scores *qi', q0'*, *qh*, respectively. Let *qr* be the quality of life for restored patients. Without loss of generality, we assume that qi<qO<qr.
   b. Transitions:
      i. a patient that follows an inpatient rehab has the following probability to pass to an outpatient regime:
      $p(I,0,t) = 1$ if t=S and x'(t)=q0
      $p(I,0,t) = 0$ Otherwise
      $p(I,H,t) = 1$ if t=S and x'(t)= qh
      $p(I,H,t) = 0$ $otherwise$
      $p(I,I,t) = 1 - p(I,0,t) - p(I,H,t)$
      ii. the probability to pass from a outpatient regime O to a restored conditions R is given by:
      $p(O,I,t) = 1$ if t=S+So and x'(t)<qo
      $p(O,I,t) = 0$ if otherwise
      $p(O,H,t) = 1$ if t=S+So and x'(t)=qh
      $p(O,H,t) = 0$ if otherwise
      $p(O,R,t) = 1$ if t=S+So and x'(t)=qh
      $p(O,R,t) = 0$ otherwise
      iii. the probabilities to pass from an at home regime H to the other conditions are given by:
      $p(H,I,t) = 1$ if t=S+Sh and x'(t) <q0
      $p(H,I,t) = 0$ otherwise
      $p(H,0,t) = 1$ I if t=S+Sh and x'(t)=q0
      $p(H,0,t) = 0$ otherwise
      $p(H,R,t) = 1$ if t=S+Sh and x'(t)=qr
      $p(H,R,t) = 0$ otherwise
      $p(H,H) = 1 - p(H,R,t) - p(H,I,t) - p(H,0,t)$

Table 12 Variables of the two Markov models.

Description	Traditional rehab model	New robotic rehab model
Direct per session costs	ci= inpatient session cost; c0= outpatient session cost	ci'= inpatient session cost, c0'= outpatient session cost; ch= at home session cost
Direct non-health per session costs	dnci: direct non-health costs inpatient session dnc0: direct non-health costs outpatient session	dnci': direct non-health costs inpatient session dnc0': direct non-health costs outpatient session dnch: direct non-health costs at home session

Indirect costs (per session)	ici: direct non-health costs inpatient session ic0: direct non-health costs outpatient session	ici': indirect costs inpatient session ic0': indirect costs per outpatient session ich: idirect costs per at home rehab session
Effectiveness	x(t)	x'(t)
Threshold for outpatient rehab	qo	
Threshold for at home rehab	qh	
Threshold for restored health	qr	
Transitions probabilities	CMM model (*)	NMM model (*)

(*) see section 4.5.1.

4.5.2 Simulations based on probabilistic sensitivity analysis

Considering:

a) the variables presented in Table 12 and the transition probabilities expressed in the Markov models;

b) for each variable, a probability distribution based on specific parameters that mirror our current knowledge and the expected range of values assumed by the included variables in future scenarios, we can develop probabilistic models for the analysis reported in Table 12. Utilizing a Monte Carlo approach and efficient random sampling (such as the latin hypercube sampling) from the defined distributions, we can:

- assess the sensitivity of indicators for robotic-rehab cost-effectiveness (such as IER, ICUR, etc.) to changes in the considered parameters (sensitivity analysis);
- assess the probability that the proposed technological solutions and new healthcare pathways are cost-effective;

In fact, the result of a probabilistic sensitivity analysis is a set of values for the model that integrates all the involved parameters. For example, consider the case of ICER of robotic rehab solutions compared with the standard of care. The probabilistic sensitivity analysis produces a set of values for ICER ($\frac{\Delta C}{\Delta E}$ where ΔC is the difference of costs between new and conventional rehabilitation, ΔE is the difference of effectiveness between new and conventional solutions) and the value of the cumulative distribution function fixed at zero F(0) offers the probability that ICER is negative, that is the proposed technological solution is cost-effective.

5 ACCEPTABILITY, USABILITY

Health technology acceptability and usability influence the successful adoption and effective use of health technology.

5.1 HOW TO ASSESS ACCEPTABILITY AND USABILITY

Several measures are commonly used to assess acceptability and usability. These dimensions correspond with the dimensions and the related validated questionnaires selected and reported in Deliverables 3.1 and 3.2. They are:

- Perceived Usefulness: the extent to which users believe that a particular technology will enhance their performance or productivity in achieving specific tasks or goals.
- Perceived Ease of Use: the degree to which users perceive a technology to be free from effort or complexity in its use. It includes aspects such as ease of learning, ease of navigation, and clarity of user interfaces.
- User Satisfaction: the overall satisfaction levels of users with a technology. It considers factors such as functionality, reliability, responsiveness, and user experience.
- Task Performance: how well users can accomplish specific tasks using the technology. This includes measures such as task completion time, error rates, and task success rates.
- Learnability: how easily users can learn to use a technology effectively. It includes measures such as time required to learn basic functions, ease of understanding instructional materials, and user feedback during the learning process.
- Effectiveness: the degree to which users can achieve their goals using the technology. It includes measures such as accuracy, completeness, and quality of outcomes achieved with the technology.
- Error Rate: the frequency and severity of errors made by users when interacting with the technology. It includes measures such as frequency of user errors, severity of errors, and impact on task performance.
- User Engagement: the level of user involvement, interest, and emotional attachment to the technology. It includes measures such as frequency of use, duration of use, and subjective perceptions of enjoyment or interest.
- Adoption Intention: users' willingness and intention to adopt and continue using the technology in the future. It includes measures such as intention to use, intention to recommend, and perceived compatibility with existing practices or systems.
- Perceived Trust: users' confidence and trust in the reliability, security, and privacy of the technology. It includes measures such as perceived security, privacy controls, and trustworthiness of the technology provider.
- User Experience: overall experience of users when interacting with the technology. It includes measures such as ease of use, satisfaction, engagement, aesthetics, and emotional response.

These measures can be assessed through various methods, including surveys, interviews, observations, usability testing, user feedback, and neuroscientific tools such as EEG. For example, band alpha-asymmetry can measure attraction or repulsion with respect to received stimuli).

5.2 ADVANCED LABORATORY INTEGRATION FOR ROBUST USABILITY AND ACCEPTABILITY EVALUATION

As we continue to develop robotic rehabilitation technologies, establishing a methodical framework for testing and refining these innovations is crucial. We are currently integrating a state-of-the-art laboratory equipped with advanced neuroscientific and biometric tools. This facility is being set up to replicate various real-world settings and will play a crucial role in our comprehensive usability and acceptability assessment process. By providing invaluable insights that drive user-centered technology enhancements, this section details our approach to utilizing these sophisticated laboratory resources. This setup is designed to ensure that our technologies are not only innovative but also closely aligned with user comfort, safety, and efficiency, developing in parallel with the compilation of this deliverable.

5.2.1 Objective and Framework

As part of our ongoing development of robotic rehabilitation technologies, we are establishing a specialized laboratory within the Center of Excellence IURAT designed to mirror real-world settings where these technologies will be applied. This laboratory is equipped with advanced neuroscientific and biometric tools, such as EEGs, motion capture systems, and eye-tracking devices, which are crucial for capturing a wide spectrum of user interactions with the technologies.

Our objective with this setup is to meticulously observe and analyse both explicit behaviours and subtle physiological responses during technology usage. This data is vital for understanding user experience in depth, which directly feeds into an iterative design process. By doing so, we aim to continually refine our technologies to enhance both their usability and acceptability among diverse user groups. This framework ensures that as the laboratory is developed, it integrates seamlessly into our broader project goals, complementing and enhancing our existing research and development activities.

5.2.2 Simulation of Real-World Environments

In our specialized laboratory, we are constructing environments that accurately reflect the typical settings where rehabilitation technologies will be utilized, such as patients' homes and various clinical contexts. These controlled yet varied simulations are fundamental to testing the technologies under conditions that closely mimic their intended use. Each setting within the laboratory is equipped with modular elements that can be adjusted to cater to different therapeutic requirements and user demographics. This flexibility allows us to thoroughly assess how each technology performs in terms of ease of integration into daily routines, as well as its adaptability to different care environments. By meticulously evaluating these scenarios, we are able to pinpoint and refine design elements that significantly contribute to enhancing user comfort, ensuring safety, and facilitating intuitive interaction with the technologies. This rigorous testing process helps ensure that the rehabilitation solutions are not only functional and effective but also user-friendly and conducive to positive user experiences in realistic settings.

5.2.3 Data Collection and Analysis

To capture comprehensive data on how users interact with our rehabilitation technologies, we employ a suite of sophisticated tools within our laboratory setup. EEGs are utilized to monitor and record brain activity, providing insights into the cognitive load and emotional responses users experience during technology use. This data helps us understand the mental effort required to operate the technology and the emotional impact it has on users. Eye-tracking technology complements this by monitoring the visual attention of users, revealing how they navigate the technology's interface and highlighting elements that either capture attention effectively or lead to confusion. Additionally, wearable sensors are used to track physiological responses and movements, offering a continuous stream of data that contributes to a holistic understanding of user interaction. This integration of diverse data collection methods ensures a comprehensive analysis of user engagement, guiding us in refining technology design to better meet user needs and enhance overall usability.

5.2.4 Usability Studies and User Feedback Integration

Our approach to refining rehabilitation technologies is heavily based on direct input from end-users. We conduct structured usability studies that not only observe user interactions in a controlled environment but also gather in-depth qualitative feedback through subsequent interviews and focus groups. These discussions are essential for understanding user experiences beyond quantitative measures, allowing us to delve into personal perceptions and detailed accounts of technology usage. Participants are encouraged to express their thoughts on the interface design, ease of use, and the personal relevance of the technology features. This qualitative feedback is invaluable for identifying not just functional aspects of the technology but also emotional and psychological impacts. Each session is meticulously analyzed to extract actionable insights, which are then used to tailor the technology to better align with user expectations and preferences, enhancing both the practical and personal usability of our rehabilitative solutions.

5.2.5 Multidisciplinary Collaboration and Iterative Design

Our laboratory serves as a nexus for multidisciplinary collaboration, engaging experts from the fields of engineering, healthcare, psychology, and design to foster a holistic evaluation of new rehabilitation technologies. This integrative approach allows for a diverse range of insights and expertise to influence the development process. Specialists from each discipline work together to analyze data, assess functionality, and ensure the technologies meet the nuanced needs of users from various backgrounds. Regular iterative design sessions are integral to our process, wherein the team collectively reviews feedback and performance data to identify potential enhancements. These sessions facilitate dynamic adjustments to design and function, with the aim of refining user interface, increasing accessibility, and enhancing overall satisfaction. This cyclic process of review and modification continues throughout the development

phase to ensure that the final products not only meet clinical requirements but also excel in user engagement and satisfaction.

5.2.6 Assessing the Theoretical Framework in the Laboratory

In our laboratory, the rigorous assessment of the theoretical frameworks that underpin our rehabilitation technologies is a key component of our research process. This evaluation ensures that our practical applications are not only grounded in robust scientific principles but also continually refined based on empirical data. By systematically testing these theoretical models against real-world data collected in simulated environments, we identify areas where our understanding needs to be adjusted or expanded. This iterative process allows us to align our technological innovations more closely with the latest scientific research and clinical practices, ensuring that each advancement in technology is both theoretically sound and practically effective. This holistic approach reinforces the lab's role as a critical nexus where theory and practice converge, driving innovations that are deeply informed by both empirical evidence and theoretical rigor.

5.2.7 Training and Workshops

To ensure the efficacy of our technological assessments and the successful implementation of our findings, comprehensive training sessions and workshops are organized regularly within our laboratory environment. These educational initiatives are designed to equip all project participants—including designers, engineers, healthcare professionals, and technical staff—with advanced skills in handling and interpreting the sophisticated data collection tools used in our studies. The training covers various aspects, from operational procedures of the equipment to advanced data analysis techniques, fostering a deep understanding of both the theoretical and practical components of our research. By enhancing the team's proficiency, we ensure that the insights garnered from the laboratory are accurately understood and effectively applied to the technology development process. These sessions not only build technical capacity but also enhance interdisciplinary communication and collaboration, which are crucial for the iterative design and continuous improvement of our rehabilitation technologies.

6 Organizational issues and Diagnostic and Therapeutic Care Pathways (DTCP)

Although the assessment of the organizational changes induced by medical devices is mandatory for forecasting and mitigating barriers that will reduce the practical use of technology, there are no methodological standards, and the available techniques are not sufficient. Assessing organizational changes induced by medical devices involves evaluating various aspects of an organization's operations, including processes, workflows, culture, and performance. Some methods commonly used for assessing such changes are:

- Surveys and Questionnaires collect feedback from employees regarding their expectations and effective experiences with the new medical devices about changes in workflow, ease of use, perceived benefits, and any challenges faced.
- Interviews and Focus Groups discussions with key stakeholders. They include healthcare providers, administrators, and support staff. This qualitative approach can provide valuable insights into the impact of medical devices on organizational dynamics.
- Observational Studies on how medical devices are being used in real-world clinical settings. This method allows researchers to understand how devices integrate into existing workflows and identify areas for improvement.
- Key Performance Indicators (KPIs) such as patient outcomes, staff productivity, and cost-effectiveness, are included in the analysis to measure the impact of medical devices on organizational performance pre and post introduction of the device.
- Analysis of data generated by medical devices, such as usage patterns, error rates, and downtime. This can help identify trends and areas where additional training or support may be needed.
- Change Impact Assessment: change impact assessments, evaluates the effects of medical devices on different aspects of the organization, including processes, roles, and responsibilities.

● Culture and Climate Surveys: assess the organizational culture and climate to gauge how the introduction of new medical devices has influenced attitudes, beliefs, and behaviors within the organization.
● Quality Improvement monitoring. Continuous monitoring of the changes in the level of quality (obtained through questionnaires) induced by the medical devices.
● Benchmarking: comparing the organization's performance and practices with industry benchmarks or best practices to identify areas of strength and opportunities for improvement related to the use of the medical devices.
● Mathematical approaches such as optimization, queue theory, Discrete event simulation (DES) can offer a simulation of the impact of robotic rehab within organizations and for different rehab regimes.

The design of Diagnostic and Therapeutic care pathways involving robotic rehab technologies and the assessment of their organizational impact will employ a combination of the following methods:

- Operational (or operations) Research (OR) is a field of study that uses advanced analytical methods to make better decisions and optimize complex systems. In healthcare organizations, OR plays a crucial role in improving efficiency, resource allocation, patient care, and overall performance. The key areas where OR is applied in healthcare organizations are:

● Resource Allocation: OR techniques are used to optimize the allocation of resources such as staff, equipment, beds, and medications. This involves developing mathematical models to match supply with demand, minimize costs, and maximize the utilization of resources while maintaining quality of care.
● Scheduling and Capacity Planning: OR methods help healthcare organizations in scheduling appointments, surgeries, tests, and other procedures to minimize wait times, reduce bottlenecks, and maximize the use of facilities and staff resources.
● Supply Chain Management: OR is applied to manage and optimize the healthcare supply chain, including inventory management, distribution logistics, and procurement processes. This ensures the availability of essential medical supplies and reduces wastage and stockouts.
● Patient Flow and Process Improvement: OR techniques are used to analyse patient flow through healthcare systems, including emergency departments, outpatient clinics, and hospitals. By identifying inefficiencies and bottlenecks, OR helps in redesigning processes to improve throughput, reduce waiting times, and enhance patient satisfaction.
● Healthcare Delivery Models: OR is used to evaluate different healthcare delivery models, such as telemedicine, home care, and integrated care systems. Mathematical modelling helps in assessing the impact of these models on cost, quality, and accessibility of healthcare services.
● Healthcare Analytics and Decision Support: OR techniques are applied to analyse healthcare data, including electronic health records, clinical data, and administrative data. This helps in identifying patterns, trends, and correlations, as well as making predictions and recommendations to support clinical and managerial decision-making.
● Healthcare Policy and Planning: OR is used to inform healthcare policy decisions and strategic planning initiatives. Mathematical modelling and simulation help in assessing the potential impact of policy interventions, such as changes in reimbursement systems, healthcare regulations, and public health initiatives.
● Patient Safety and Quality Improvement: OR methods are applied to enhance patient safety and quality of care by optimizing processes, reducing medical errors, and implementing evidence-based practices. This includes techniques such as queuing theory, risk analysis, and optimization of clinical pathways.

OR plays an important role in improving the efficiency, effectiveness, and quality of healthcare delivery by applying rigorous analytical methods to address complex challenges faced by healthcare organizations. This approach can be adopted to design and assess the organizational changes that each involved healthcare facility and organization should implement to boost the adoption and diffusion of robotic rehabilitation.

- Balanced Scorecard (BSC): The balanced scorecard is a strategic performance management framework that translates an organization's strategic objectives into a set of balanced performance measures across the following perspectives: financial, customer, internal processes, and learning and growth. Additional analyses quantify the relationships between these perspectives.
- Data Envelopment Analysis (DEA): DEA is a mathematical technique used to assess the relative efficiency of decision-making units (departments, branches, organizations) by comparing their inputs and outputs. It allows organizations to benchmark their performance against peers and identify areas for improvement (Cooper et al. 2007). However, the approach has some limitations:

- It identifies inefficiencies, but it does not provide specific guidance on how to improve performances.
- It is sensitive to the choice of inputs and outputs.
- It assumes that all units operate under the same production technology.
- It does not account for external factors or environmental conditions that affect efficiency.

- Discrete Event Simulation (DES) is a computational modelling technique used to model and analyse systems where events occur at distinct points in time and space, and where system state changes only at those event times. These systems are characterized by the presence of queues, resources, and stochastic events. (Caro 2005; 2016) Applied in the healthcare sector, DES allows analysts to study system behaviour, assess performance metrics (throughput, waiting times, resource utilization, etc.), and evaluate the impact of changes or improvements to the system without the need for costly real-world experimentation. DES models can range from simple representations of basic systems to complex models of large-scale, intricate systems. Popular software tools for Discrete Event Simulation include Simul8, Arena, AnyLogic, ExtendSim, and ProModel, among others. These tools provide graphical interfaces for building, running, and analysing DES models.

Tools and instruments for assessing the organizational impact of both current and new healthcare pathways will be selected according to the following principles:

- Specificity: Each combination of tools should be personalized for a specific system of solutions/technologies.
- Appropriateness: The selection of tools will prioritize starting with the simplest yet effective options before considering more complex ones.
- Accessibility: Regardless of the complexity of the selected tools, the goal will be to define criteria for translating the outcomes of the chosen approach into accessible language useful for the decision-makers involved.

7 ETHICAL AND LEGAL BARRIERS

Ethical and legal barriers are extremely relevant for the successful transfer of robotic rehabilitation solutions to clinical practice and to favour the development of a competitive industry of robotic rehabilitation technologies. For a detailed analysis of these dimensions, we refer to deliverables produced by colleagues of Action 4 (Mission 1).

In order to highlight the importance of the regulatory and legal barriers for the design of sustainable business models and plans, together with A4, we have set up a working group composed by relevant internal and external stakeholders (we started with internal ones – the companies partners of Fit4medRob Initiative - and we are in the process of opening the participation also to stakeholders external to the partnership, such as representatives of industrial organizations, managers of healthcare facilities, representatives of scientific societies, representatives of regulatory agencies). This multidisciplinary working group will provide different perspectives on legal, regulatory and ethical barriers, and enabling factors for the creation of a favourable innovation ecosystem, the building of solid industry in robotic and allied technologies, and the design of sustainable business models.

8 INTEGRATION OF HTA IN THE CURRENT FIT4MEDROB CLINICAL TRIALS

The HTA approach presented in previous sections has been included in the protocols of several Studies designed by the clinical Partners of Fit4MedRob project in the last months. Below some of those and the role that SSSA (Activity 3) has played in contributing to the trials' protocols design are highlighted.

8.1 STUDY (1): STROKE

Within Fit4MedRob, the HTA approach has been applied to assess and compare multimodal, neuromotor and cognitive rehabilitation, with (study group) and without (control group) Robots and Digital Technologies (RADTs) in patients with

stroke. The associated clinical study is a multicenter randomized controlled. Twelve centres will enroll and rehab patients.

Clinical and nonclinical outcomes

The primary endpoint is the effectiveness of rehabilitation.

Effectiveness will consist of a series of measures able to assess the patient's recovery of autonomy.

The rate of recovery over the treatment will be assessed by the following tests conducted every 5 treatment sessions:

- The Box and block test.
- The 10 meters walk test.

In addition, the following tests will be also adopted.

- Fugl-Meyer Assessment for the upper extremities.
- Fugl-Meyer Assessment for the lower extremities.
- Berg Balance Scale (balancing and equilibrium).
- The Symbol Digit Modalities Test (cognitive dimension).

Other considered dimensions will be:

- Body function, measured through:
  - the Modified Ashworth Scale
  - the Motricity Index (upper and lower extremities and trunk);
  - the numerical Rating Scale for Pain;
  - the Douleur Neuropathique questionnaire;
- Action of patient measured through:
  - the research Arm test;
  - the 2 Minute Walk Test.
- Quality of life measured through the EQ-5D-5L questionnaire (see the deliverable dedicated to eCRF).

As one can see, both clinical and nonclinical dimensions are utilized to measure the improvement of patients' conditions before and after rehabilitation training.

The secondary endpoints include the acceptability, usability, and economic-organizational sustainability of RADTs, spanning from the subacute to chronic phases.

Given that the study will evaluate the impact of RADTs not only from the perspective of patients, their families, and payers, but also from that of healthcare professionals, the multidimensionality and multiperspective nature of the adopted measures align with the principles of HTA.

8.1.1 Acceptability and usability of technologies

The study and control groups will also include a cohort of healthcare workers involved in rehabilitation. They will be requested to complete customized questionnaires pertaining to:

- Quality of work.
- Confidence and familiarity with ICT technologies.
- Acceptability and usability of the technology solutions.

Acceptability and usability will be also evaluated for patients, who will be asked to complete specific questionnaires.

8.1.2 The Economic dimensions

To conduct cost-effectiveness, cost-utility, and budget impact assessments, the study will evaluate several cost dimensions.

Type of costs:

- **Direct healthcare costs**:

- Unit costs of the technology per session (including the cost of the technology, depreciation rates based on the estimated number of treated patients when centers are fully operational, maintenance costs, energy consumption, consumables, etc.).
- Unit cost of staff involved in rehabilitation sessions.
- Hospitalization costs.

- **Direct non-medical costs**, such as expenses not reimbursed by the health service related to medications, visits, transportation costs to reach the rehabilitation center, etc.
- **Indirect costs** associated with the loss of productivity for the patient and/or their family member assisting during working hours.

The analysis will consider perspectives from the patient and their family members, healthcare providers, rehabilitation centers, the Healthcare Service System, and/or other payers.

A microcosting approach will be employed for both the study and control arms, as well as reimbursement rates for the control group.

The economic outcome will consist of the ratio between the differences in clinical and non-clinical dimensions and the differences in costs for the control and study group.

Simulation tools will be adopted for assessing the medium and long-run cost effectiveness of the compared solutions.

8.1.3 The organizational impact

Key performance indicators (KPIs) of organizational type (from the perspective of the centers involved) will include:

- Average length of hospital stays.
- Patient waiting time for the first rehabilitation session.
- Bed turnover: the number of discharges in the considered timeframe divided by the number of beds in the facilities during the same timeframe.
- Bed occupancy rate: the number of occupied beds divided by the total number of beds.
- Readmission rate: the total number of readmissions divided by the total number of patients.
- Number of patients treated.
- Number of dedicated beds.
- Daily or per-session rehabilitation reimbursement by the NHS.
- Staff-to-patient ratio: the number of staff needed per patient per session.
- Space requirements (in square meters) of the facility necessary for specific treatments.
- Training time/learning curve (for caregivers or families) in supporting patients during rehabilitation sessions.
- Physical therapist's mental workload: the amount and complexity of information and decisions that physical therapists have to manage or make in each session.

8.1.4 Dimensions, questionnaires, and involved stakeholder

The general scheme of the types of dimensions that will be assessed beyond the clinical ones and the involved stakeholders is reported in Table 13.

Table 13 Dimensions, questionnaires, and involved stakeholder.

Dimensions	Sub-dimension	Questionnaires	Stakeholders involved	Studies involved
Acceptability and usability	Perception of usefulness	TAM (technology acceptance model)	Patiens, families, healthcare professionals, administrative staff of hospital facilities	(1), (2), (3)
	Ease of use Compatibility			
	Intention to use			
	Questions regarding needs, available solutions, and perception of relative complexity	Ad hoc questionnaires consisting of open questions		
Quality of work	Working related quality of life	WRQoL (working-related quality of work)	Healthcare professionals	(1)
ICT and computer skills	Availability of ICT tools Frequency of use	The Computer Skills Questionnaire	healthcare Patiens, families, professionals	(1)
	Digital skills (Information searching, Communication, Content creation, Security, Troubleshooting)			
Costs	Direct health, direct non-health, indirect	Ad hoc questionnaire	Patiens, families	(1), (2), (3)
Organizational KPIs	See Table 1.7		Administrative staff of hospital facilities	(1)

Study (1) is described in section 8.1, Study (2) refers to section 8.2. For more details on Study (3) see section 8.3.

8.2 STUDY (2): PEDIATRIC UPPER-LIMB REHABILITATION

A second application of the dimensions of Health Technology Assessment (HTA) lies in its integration into a multicenter case-control pilot study concerning Pediatric Upper Limb Rehabilitation using a modular bilateral end-effector device: PhiCube-Pediatric. This study aims to explore the feasibility and efficacy of a treatment for upper limb function in children aged 4-18 with congenital and acquired neuromotor disorders, utilizing a novel wearable robotic system designed for bilateral upper limb neuromotor rehabilitation. PhiCube assists clinicians in upper limb rehabilitation, while PhiCube-Pediatric enables interactive robotic therapy for addressing deficiencies in upper limb mobility and motility resulting from conditions such as congenital or acquired brain injury, motor coordination disorder (DCD), and other diseases requiring upper limb rehabilitation.

The HTA approach mirrors that of Study (1), as outlined in Table 1.13. The primary deviation lies in the absence of questionnaires concerning the ICT (Information and Communication Technology) and computer skills of families. However, when children are the subjects, assessing these dimensions via validated questionnaires presents challenges due to the participants' age and cognitive capabilities. In such cases, parents will respond to the selected questionnaires on behalf of their children.

An additional challenge pertains to the absence of productivity loss data, particularly in terms of the working days lost by parents to care for their children and the school days missed by the children themselves. Here, productivity loss encompasses both parental absence from work to assist their children and the children's absence from school.

8.3 STUDY (3): A PRAGMATIC STUDY FOR TESTING AN INNOVATIVE PATHS TO PAEDIATRIC CARE WITH MULTI-DOMAIN TECHNOLOGICAL AND ROBOTIC REHABILITATION

The third trial, coordinated by IRCCS Fondazione Stella Maris, in which dimensions of the HTA approach will be integrated with the clinical dimensions is a pragmatic multicentric study that tries to comprehensively and accurately evaluate the effectiveness of robotic and technological system-assisted rehabilitation. The objective of the study is to evaluate, in a pragmatic trial of a large sample of paediatric patients (5-21 years old) with congenital or acquired neuromotor disorder, the effectiveness and cost-effectiveness of a multimodal treatment making use of robotics and advanced technologies compared to a single-domain treatment using a single technological or robotic device. In more details, all patients involved in the study will receive conventional therapies plus robotic sessions assisted by robotic and technological devices. Two groups are considered. In the first group (active control) only one technology will be required and will focus on a single rehabilitative function; in the second group (experimental) multiple technologies providing a multi-domain intake also through innovative systems will be used. See Table 6.1.4 for the selected dimensions.

8.4 ROLE AND CHARACTERISTICS OF HTA ACTIVITIES IN THE PROGRAMMED PRAGMATIC CLINICAL TRIALS

The three cases reported in this section 6 mark the beginning of a series, involving integrations and adaptations of HTA tools, models, and approaches, according to the different robotic technologies, types of rehabilitation, characteristics of stakeholders and involved diseases. These integrations and adaptations will be applied to some of the currently 15 programmed pragmatic clinical trials of Fit4MedRob, and on some of the eventual other studies that will be designed in the next months.

Table 14 Role and characteristics of HTA activities in the programmed pragmatic clinical trials.

Target group	Setting	Sample size	Title	Objective	PI	HTA		
						Involved stakeholders	Considered non-clinical dimensions*	Type of studies
Post-stroke patients	clinical setting	596	Multimodal, Neuromotor, and Cognitive Rehabilitation, With and Without Robots and Digital Technologies (RADTs), in Patients after Stroke: A Multicenter Randomized Controlled Clinical Study on the Efficacy on Activities of Daily Living recovery, Acceptability, Usability, and Economic-Organizational Sustainability of RADTs, from Subacute to Chronic Phase. STROKEFIT4.	To demonstrate the non-inferiority of a multimodal rehabilitation intervention using robotic and technological devices compared to traditional rehabilitation treatment in the recovery of activities of daily living in patients with stroke.	Irene Giovanna Aprile (IRCCS Fondazione Don Carlo Gnocchi)	Patients, their families, healthcare professionals, hospital facilities	PREMS, PROMS, Organizational KPIs. Acceptability, Usability, Direct and indirect costs	CEA, CUA, BIA
Patients with Parkinson Disease or Multiple Sclerosis	home-based setting	300	Effectiveness of TeleNEUROrehabilitation systems for timely and personalized interventions and vigilant care in neuro-degenerative conditions: the FIT4TeleNEURO pragmatic trial.	To determine the effectiveness of telerehabilitation systems for patients with neurodegenerative conditions.	Francesca Baglio (IRCCS Fondazione Don Carlo Gnocchi)	patients, their families, healthcare professionals	PROMS Acceptability, Usability, ICT skills and availability of ICT infrastructures, Direct & indirect costs	CEA, CUA, BIA
Patients with Severe Acquired Brain Injury	clinical setting	198	Multicentric study on combined robotic verticalization and mobilization in patients with severe acquired brain injury: A randomized controlled trial. VEM in sABI.	To determine the effectiveness of robotic verticalization combined with lower limb mobilization compared to standard verticalization in promoting short recovery of cognitive functioning/consciousness.	Anna Estraneo (IRCCS Fondazione Don Carlo Gnocchi)	patients, their families, healthcare professionals, hospital facilities	PREMS, PROMS, Organizational KPIs. Acceptability, Usability, Direct and indirect costs	CEA, CUA, BIA
Patients with Severe Acquired Brain Injury	clinical setting	28	Multicentric study on implementation of Virtual Reality for rehabilitation of cognitive functions in patients with severe acquired brain injury: A randomized controlled trial. VR in sABI.	To explore the efficacy of a rehabilitation treatment based on Virtual Reality systems.	Anna Estraneo (IRCCS Fondazione Don Carlo Gnocchi)	patients, their families, healthcare professionals, hospital facilities	PREMS, PROMS, Organizational KPIs. Acceptability, Usability, Direct and indirect costs	CEA, CUA, BIA
Frail Elderly and workers	clinical setting	50	Virtual Reality for Musculoskeletal Disorders: REVISA.	To assess the level of acceptability and usability of a VR system during the execution of several rehabilitation exercises.	Umile Giuseppe Longo (Fondazione Policlinico Univers Campus Bio-Medico)	patients, their families, healthcare professionals, hospital facilities	PREMS, PROMS, Organizational KPIs. Acceptability, Usability, Direct and indirect costs	CEA, CUA, BIA
Frail Elderly	clinical setting	100	Comparison between treatment with sensorised treadmill and conventional therapy in balance disorders and use of Artificial Intelligence in identifying predictive and prognostic indices of the risk of falling in balance disorders in adult-elderly subjects. UAI.	To evaluate an improvement in the personalized fall predictive index, using Artificial Intelligence models, in order to prevent falls in the elderly.	Federica Bressi (Fondazione Policlinico Universitario Campus Bio-)	patients, their families, healthcare professionals, hospital facilities	PREMS, PROMS, Organizational KPIs. Acceptability, Usability, Direct and indirect costs	CEA, CUA, BIA
Frail Elderly	clinical setting	30	Role of nutritional status in functional recovery of older adults undergoing virtual reality-augmented shoulder rehabilitation: NEFAP trial.	To showcase malnutrition's impact on ability in daily activities (i.e. functional recovery) after rehabilitation for shoulder elective surgery.	Claudio Pedone (Fondazione Policlinico Universitario Campus Bio-Medico)	patients, their families, healthcare professionals, hospital facilities	PREMS, PROMS, Organizational KPIs. Acceptability, Usability, Direct and indirect costs	CEA, CUA, BIA
Patients with polyneuropathies	clinical setting	100	Evaluation and rehabilitation of patients with peripheral neuropathy with static and dynamic stabilometric platform: NEUROSTAB.	To evaluate the actual potential use and effectiveness of a static and dynamic stabilometric platform.	Angelo Schenone (IRCCS Ospedale Policlinico San Martino)	patients, their families, healthcare professionals, hospital facilities	PREMS, PROMS, Organizational KPIs. Acceptability, Us ability, Direct and indirect costs	CEA, CUA, BIA
Patients with Cerebral Palsy	clinical setting	194	Innovative Paths to Paediatric Care: A Multicenter Study on the Efficacy of Multi-Domain Technological and Robotic Rehabilitation. TECHildren REHAB.	To demonstrate the effectiveness of an integrated rehabilitative treatment utilizing robotic and/or technological devices compared to a treatment focused on a single domain using only one technological or robotic device.	Giuseppina Sgandurra (IRCCS Fondazione Stella Maris)	patients, their relatives, healthcare professionals, hospital facilities	PREMS, PROMS, Organizational KPIs. Acceptability, Usability, Direct and indirect costs	CEA, CUA, BIA
Patients with Cerebral Palsy	home-based setting	40	Demonstrate the clinical improvement due to the home use of Agilik in children with Cerebral Palsy: Agilik@home.	To improve the clinical use of a powered knee-ankle-foot orthosis that is tailored on the patients anthropometric features and gait pattern in a home-based setting.	Emilia Biffi (IRCCS Eugenio Medea)	patients, their families, healthcare professionals	PROMS Acceptability, Usability, ICT skills and availability of ICT infrastructures, Direct and indirect costs	CEA, CUA, BIA
Oncology patients	clinical setting	50	The ICT based prescription of Physical Activity for oncology patients at their home: the EASYDOM trial.	To assess the effectiveness of an adapted physical activity program with technological monitoring in reducing cardiovascular risk, compared to an adapted physical activity program without technological monitoring.	Guido Iaccarino (Università degli Studi di Napoli Federico II)	patients, their families, healthcare professionals, hospital facilities	PROMS, Organizational KPIs. Acceptability, Usability, Direct and indirect costs	CEA, CUA, BIA

Frail Elderly	clinical setting	40	Frail Elderly with Femur Fractures: Rehabilitation with and without Allied Technology. FEWF.	To assess the effectiveness of a technological rehabilitation treatment in the recovery of lower limb functional impairment.	Ennio Ferlazzo (Istituto Clinico Polispecialistico COT)	patients, their families, healthcare professionals, hospital facilities	PREMS, PROMS, Organizational KPIs. Acceptability, Usability, Direct and indirect costs	CEA, CUA, BIA
Post-stroke patients	home-based setting	160	Telerehabilitation using Digital tools for the continuum of care in stroke patients: a multicenter RCT on the effectiveness, acceptability, usability, and economic sustainability. STROKEFIT4HOME.	To demonstrate the superiority of a home-based multimodal rehabilitation treatment based on technological devices over traditional home-based rehabilitation treatment in the recovery of balance.	Irene Giovanna Aprile (IRCCS Fondazione Don Carlo Gnocchi)	patients, their families, healthcare professionals	PREMS, PROMS, Organizational KPIs. Acceptability, Usability, Direct and indirect costs	CEA, CUA, BIA
Patients with Neuromuscular diseases (polyneuropathies, amyotrophic lateral sclerosis, muscular dystrophies)	clinical setting	90	Clinical Protocol for a Pragmatic Trial on a High-Tech Rehabilitation Pathway for Acute and Chronic Adult Neuromuscular Diseases: Fit4MedRob-MN project.	To evaluate the effectiveness of a multimodal rehabilitation intervention based on robotic and technological devices in the recovery of trunk control and gait in patients with neuromuscular diseases	Christian Lunetta (IRCCS Istituti Cli Scient Maugeri) Angelo Schenone (IRCCS Ospedale Policlinico San Martino)	patients, their families, healthcare professionals, hospital facilities	PREMS, PROMS, Organizational KPIs. Acceptability, Usability, Direct and indirect costs	CEA, CUA, BIA
Post-stroke patients	clinical setting	30	Bilateral Upper-limb robotic training in chronic stroke: Influences of Lesion site on Treatment response BUILT.	To investigate the effectiveness of a robotic bilateral exoskeleton on chronic stroke to highlight any differences in the response to treatment related to lesion location in the dominant or non-dominant hemisphere.	Carmelo Chisari (Università di Pisa)	patients, their families, healthcare professionals, hospital facilities	PREMS, PROMS, Organizational KPIs. Acceptability, Usability, Direct and indirect costs	CEA, CUA, BIA

* The list of selected disease and stakeholder specific and generic questionnaires is reported in Deliverable 3.2. CEA: cost-effectiveness analysis, CUA: cost-utility analysis, Budget Impact analysis.

9. PART II EHTA

This section presents the most relevant tools and strategies for assessing and simulating the expected value and future impact (that is the economic and organizational sustainability, acceptability, ease of use, etc.) of robotic rehabilitation solutions among the final users, healthcare professionals, patients, and their families. These tools are typically adopted from the **early stages of technology integration/production** to increase the probability that the developed technology, once in the market, will be sustainable and eligible for reimbursement.

10. EHTA IN THE REHAB ROBOTIC R&D PROCESS: CHALLENGES AND LIMITS WITHIN THE COMPANIES

10.1 EHTA DEFINITIONS AND DIMENSIONS

Early-stage Health Technology Assessment (HTA) of biomedical devices requires different methods than those usually employed for pharmaceuticals. This section discusses their limits for early-stage evaluation of biomedical devices and presents two methods for early stage HTA being developed in the Multidisciplinary Assessment of Technology Centre for Healthcare (MATCH) project: Analytic Hierarchy Process (AHP) to elicit user needs.

Early health technology assessment is increasingly being used to support health economic evidence development during early stages of medical product development. These early models can inform research and development about the design and management of new medical technologies, associated with market access and reimbursement. Over the past 25 years, it has been suggested that health economic evaluation in the early stages may benefit the development process.

The most frequently used methodology in early health technology assessment is early-stage (or iterative) health economic modeling. Further methodological development is required by combining systems engineering and health economics to manage uncertainty in medical product portfolios.

The Analytic Hierarchy Process (AHP) is a method for organizing and analysing complex decisions, using math and psychology. It was developed by Thomas L. Saaty in the 1970s and has been refined since then. AHP provides a rational framework for a needed decision by quantifying its criteria and alternative options, and for relating those elements to the overall goal. Stakeholders compare the importance of criteria, two at a time, through pair-wise comparisons. AHP converts these evaluations into numbers, which can be compared to all the possible criteria.

Early stage HTA of biomedical devices requires different methods than those used for pharmaceuticals. The MATCH project is developing two methods for early stage HTA: AHP to elicit user needs and early-stage economic evaluations using Markov Models. Early health technology assessment is increasingly being used to support health economic evidence development during early stages of medical product development.

10.2 SELECTION OF THE VARIABLES

Selecting variables for early-stage health technology assessment (eHTA) is a crucial step in ensuring that the assessment is comprehensive and informative. The selection of variables should be based on the specific technology being assessed and the goals of the eHTA. Here are some general guidelines for selecting variables for eHTA:

1. Clinical needs: Identify the clinical needs that the technology aims to address. This includes the target patient population, the condition or disease being treated, and the current standard of care.
2. Clinical pathway positioning: Determine how the technology fits into the existing clinical pathway. This includes understanding the current treatment algorithms, the role of the technology in the care pathway, and the potential impact on patient outcomes.
3. Market sizing: Estimate the potential market size for the technology. This includes the number of patients who could benefit from the technology, the potential market demand, and the potential market share.
4. Cost-effectiveness: Assess the cost-effectiveness of the technology. This includes the cost of the technology, the potential cost savings, and the potential benefits to the healthcare system.
5. Patient preferences: Consider the preferences of the target patient population. This includes understanding their needs, expectations, and willingness to pay for the technology.

6. Regulatory requirements: Ensure that the technology meets the regulatory requirements for its intended use. This includes understanding the regulatory landscape, the approval process, and the potential impact on market access.
7. Ethical considerations: Consider the ethical implications of the technology. This includes understanding the potential risks and benefits, the impact on patient autonomy, and the potential for harm.
8. Uncertainty about the cost-effectiveness: Assess the level of uncertainty surrounding the cost-effectiveness of the technology. This includes understanding the available evidence, the quality of the data, and the potential for future research.
9. Technology lifecycle stage: Consider the stage of development of the technology. This includes understanding the current stage of development, the potential for future improvements, and the potential impact on market access.
10. Stakeholder perspectives: Consider the perspectives of all stakeholders involved in the technology development process. This includes understanding the perspectives of patients, clinicians, payers, and manufacturers.
By considering these factors, eHTA can provide valuable insights into the potential value of new technologies at an early stage of development, helping to minimize the risk of failure at later stages and optimize resource allocation.

10.3 SELECTION OF THE PERSPECTIVES - STAKEHOLDERS/PAYERS

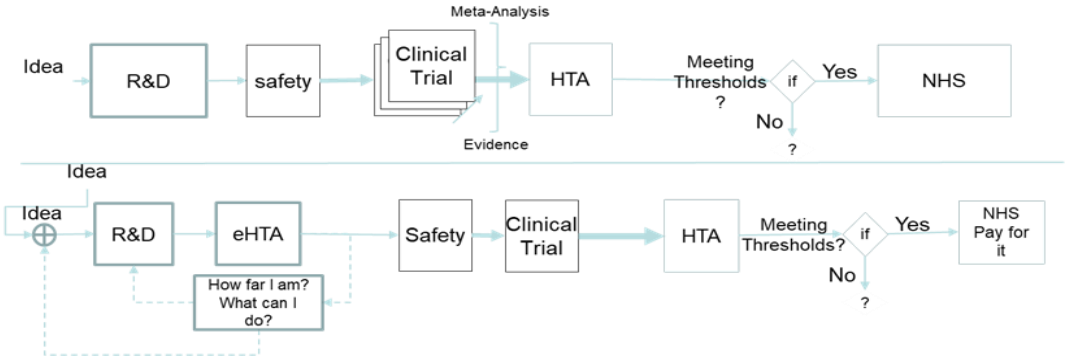


Fig. 5 Early stage HTA process (Stakeholder Perspective).

Figure 5 shows in the diagram below how early stage HTA fits into the production scheme of a medical device. In particular, there are a number of questions that the stakeholder has to ask himself during the early stages of development; moreover, being in the R&D phase, there is no evidence (other than the literature) that can help in making an accurate analysis of resource allocation. During an eHTA analysis, therefore, there are various challenges that the stakeholder has to face; the lack of evidence, makes it necessary to estimate the variables of interest.

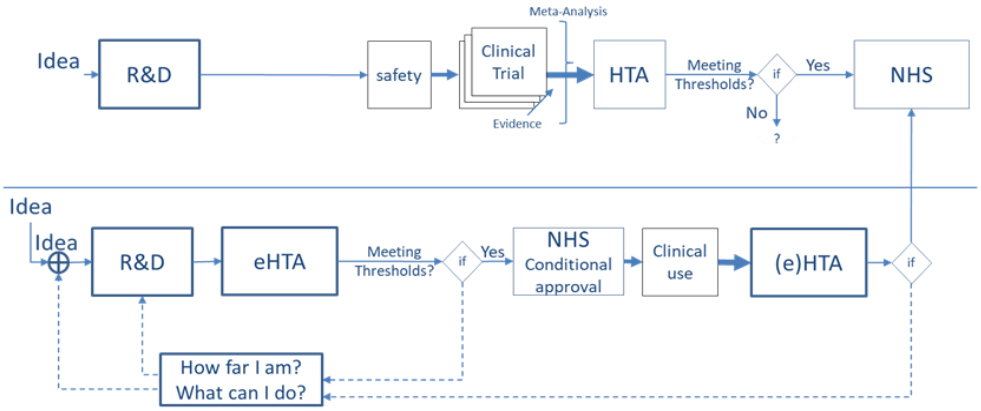


Fig. 6 Early stage HTA process (Payers Perspective).

10.4 SELECTION OF THE LEVELS OF ANALYSIS AND SOURCE OF DATA

In the realm of early-stage health technology assessment (HTA), the process of selecting the appropriate level of analysis stands as a crucial precursor to informed decision-making. This selection is contingent upon a comprehensive understanding of the assessment's distinct context and objectives. A structured approach serves as a guiding beacon in navigating this complex terrain.

First and foremost, clarity is paramount in defining the decision context and issue at hand. Articulating the specific decision to be made and contextualizing it within its broader environment lays the foundation for a targeted analysis. This clarity not only delineates the scope of inquiry but also illuminates the path towards identifying the depth of analysis required and the corresponding data and evidence necessary to support it.

Furthermore, understanding the nature of the technology under assessment is indispensable. Categorizing the medical device into its respective domain whether it be a medical device, procedure, care process, or health information system provides crucial insights into the dimensions and methodologies best suited for evaluation. This classification informs the selection of assessment metrics and methods, ensuring alignment with the unique characteristics of the technology in question.

Equally pivotal is considering the developmental stage of the MD. Recognizing the stage of development illuminates the landscape of data availability, reliability, and uncertainty. Early-stage technologies may necessitate distinct approaches compared to their more mature counterparts, warranting a nuanced evaluation methodology tailored to the specific challenges and opportunities inherent in nascent innovations.

In tandem with development stage considerations, defining the assessment dimensions is imperative. Identifying the critical dimensions for evaluation—ranging from clinical efficacy and safety to cost-effectiveness and strategic alignment provides a structured framework for analysis. These dimensions serve as touchstones, anchoring the assessment process to the overarching decision context and ensuring relevance and comprehensiveness in the evaluation process.

Furthermore, sourcing data appropriately is essential to underpin the assessment with robust evidence. Selecting pertinent and credible data sources, spanning from primary internal reports to secondary sources such as literature, surveys, and expert interviews, fortifies the assessment with a solid evidentiary foundation. This multifaceted approach to data collection ensures a holistic perspective, mitigating the risk of bias and enhancing the reliability of the assessment outcomes.

Methodological rigor is another cornerstone of effective early stage HTA. Choosing methodologies that adeptly synthesize evidence and navigate uncertainty whether through systematic reviews, expert panels, Bayesian modeling, or cost-effectiveness analyses empowers the assessment process with analytical precision and insight. These methodologies serve as analytical tools, facilitating the synthesis and interpretation of data to inform decision-making with clarity and confidence.

Moreover, considering iterative processes can enhance the adaptability and responsiveness of the assessment model. Evaluating the incorporation of iterative cycles or stop-go criteria enables dynamic decision-making throughout the assessment journey, allowing for course corrections and adjustments based on evolving insights and emerging evidence.

Mitigating cognitive biases is equally essential in ensuring the objectivity and integrity of the assessment process. Acknowledging and addressing potential biases that may influence the evaluation whether stemming from preconceived notions, vested interests, or heuristic shortcuts fosters a more objective and impartial analysis, safeguarding the validity of the assessment outcomes.

Lastly, prioritizing transparency and communication is indispensable in fostering stakeholder engagement and buy-in. Maintaining transparency throughout the assessment process and effectively communicating findings to all relevant stakeholders cultivates trust and confidence in the assessment outcomes, facilitating informed decision-making and fostering a collaborative environment conducive to innovation and progress. In conclusion, navigating the landscape of early stage HTA requires a structured and systematic approach that encompasses a myriad of considerations. By delineating the decision context, understanding the technology under assessment, considering the developmental stage, defining assessment dimensions, sourcing data appropriately, applying suitable methodologies, incorporating iterative processes, mitigating cognitive biases, and prioritizing transparency and communication, stakeholders can ascertain the most fitting level of analysis. This holistic approach ensures that the assessment is not only relevant, reliable, and rigorous but also serves as a catalyst for informed decision-making and transformative innovation in healthcare.

10.5 How to work with reduced information and small samples?

In early health technology assessment (HTA) with a reduced amount of information and small samples, Markovian models and the headroom method can be employed to perform an assessment. These methods are particularly useful when the available data is limited, and the goal is to estimate the potential future states and outcomes of a medical device.

1. Markovian models: Markovian models are a type of mathematical model that can be used to estimate the future states of a medical device or technology. They are based on the Markov property, which states that the future state of a system depends only on its current state and not on its past states. In the context of early HTA, Markovian models can be used to estimate the potential future outcomes of a medical device, such as its clinical effectiveness, safety, and cost-effectiveness. These models can be particularly useful when data is limited, as they allow for the estimation of future states based on the available information.

2. Headroom method: The headroom method is a decision-analytic tool that can be used to assess the potential value of a medical device or technology. It involves estimating the maximum amount of improvement that a new technology could provide compared to the current standard of care. This method is particularly useful in early HTA, as it allows for the estimation of the potential value of a medical device even when data is limited. The headroom method can be used to estimate the potential clinical effectiveness, safety, and cost-effectiveness of a medical device, and can help inform decision-making about whether to invest in further development or not.

Both Markovian models and the headroom method can be employed in early HTA with a reduced amount of information and small samples. These methods can help estimate the potential future states and outcomes of a medical device, even when data is limited. However, it is important to note that these methods should be used in conjunction with other sources of information and expert opinion, as they are based on assumptions and estimates that may not be fully accurate.

11. Early economic evaluations

11.1 Simulation tools: principles, perspectives and use

Simulation tools are invaluable assets in the early stages of health technology assessment (HTA), providing a structured framework for evaluating the potential impact of medical technologies. These tools empower users to construct mathematical models that mimic the intricate interactions between the technology under scrutiny, healthcare systems, and patient populations. By delving into diverse scenarios and assumptions, simulation tools assist in uncovering critical variables and uncertainties that may sway the technology's overall impact.

One of their pivotal roles lies in facilitating the estimation of cost-effectiveness. Through meticulous comparison of costs and benefits, decision-makers gain insights into the value proposition of the technology vis-à-vis existing alternatives. Furthermore, simulation tools extend their utility by projecting long-term outcomes, anticipating disease trajectories, and offering predictive analyses on the technology's lifecycle implications.

By harnessing the power of simulation, stakeholders can make informed decisions regarding resource allocation and policy development. These tools serve as decision-making aids, providing evidence-based guidance that fosters efficiency and efficacy in healthcare delivery. Additionally, simulation tools foster stakeholder engagement by offering visual representations of potential impacts and inviting feedback on model assumptions. This collaborative approach cultivates consensus and drives collective action towards innovation and improvement in patient outcomes.

In essence, simulation tools are indispensable instruments in the arsenal of early stage HTA, empowering stakeholders to navigate complexity, optimize resource allocation, and drive transformative change in healthcare delivery.

11.2 Predictive models of costs

Predictive models play a crucial role in early health technology assessment (HTA) by providing insights into the potential costs associated with implementing new healthcare technologies. Among these models, Markov models stand out for their ability to simulate dynamic processes over time, making them particularly valuable in forecasting healthcare costs. Markov models segment time into discrete intervals and transition individuals between different health states based on probabilities derived from empirical data or expert opinion. In HTA, these models enable decision-makers to assess

the long-term economic implications of adopting new technologies by estimating costs associated with various health outcomes. By incorporating factors such as disease progression, treatment effectiveness, and patient demographics, Markov models offer a comprehensive framework for evaluating the cost-effectiveness of healthcare interventions, ultimately informing resource allocation and policy decisions in the field of healthcare.

12 CASE STUDIES AS EXAMPLES OF HOW TO APPLY EHTA IN HEALTH TECHNOLOGY

By using a case-study on a fall-prediction device for elderly patients with orthostatic hypotension we aim to demonstrate how the MAFEIP tool can be used to inform manufacturers on their product development based on a cost-effectiveness criterion.

The MAFEIP allows to quickly create early economic models, and to explore model uncertainty by performing deterministic sensitivity analysis for single parameters.

In this case study, a 3-state Markov model was used including a baseline state, which represents the baseline health condition of the target population, a disease/impairment state, which reflects the health state of subjects who experience the condition of interest (for instance, an acute trauma due to a fall), and a dead state).

Each state in the model is associated with a cost, and a measure of the health-related quality of life expressed in QALYs. Model parameters, including costs and QALYs for each state and transition probabilities across states were derived from the published literature.

Since no standard healthcare technology has been identified for imminent falls prediction and prevention, the device is compared to the standard of care, to the acute management of fall-related injuries whenever they occur.

In the baseline analysis, it was assumed a cost for the device of £230 and an average lifetime of 10 years, after which replacement would be needed.

The perspective adopted for the analysis is the one of the healthcare systems, and therefore only direct health related costs and consequences are considered.

The model estimates the potential effects of using the intervention over a time horizon of 30 years, using discrete time cycles of 1 year. Lastly, a discount rate of 3.5% was applied to both future costs and consequences.

The MAFEIP tool was then applied to a novel fall-prediction device and used to estimate the expected cost-effectiveness and perform threshold analysis. In our case study, the device produced estimated gains of 0.035 QALYs per patient and incremental costs of £ 518. The estimated incremental cost-effectiveness ratio is £ 14,719, which represents the additional cost that is required to generate a health gain of 1 QALY when using the device in the target population.

Analysing the graphs obtained we will have for Fig. A, the cost-effectiveness changes that result from changing the price of the device to £130 every 15 years and to £300 every 6 years. Similar to the base case, in the sensitivity analysis the device acquisition costs were modelled as one-time costs at the beginning of the model and were assumed to be equal to 200 and 1,000 pounds, respectively, or the full discounted cost of the technology over a 30-year time horizon. With a WTP threshold of 20,000 pounds, applying the higher price would likely lead to a rejection by the payer because the resulting incremental cost-effectiveness ratio would be higher (26,000 pounds).

In contrast, for Fig. B we will have that if the actual incidence of falls in the intervention group were slightly higher than the expected value used in the reference case, it is unlikely that payers would adopt the device. In particular, even with a threshold of 20,000 pounds, an increase in incidence from 0.26 to 0.28 would make the device unaffordable. However, keeping the baseline fall probability and the percentage of falls due to OH fixed, to achieve this increase in incidence, the sensitivity of the device would have to be less than 0.45, which is rather unlikely.

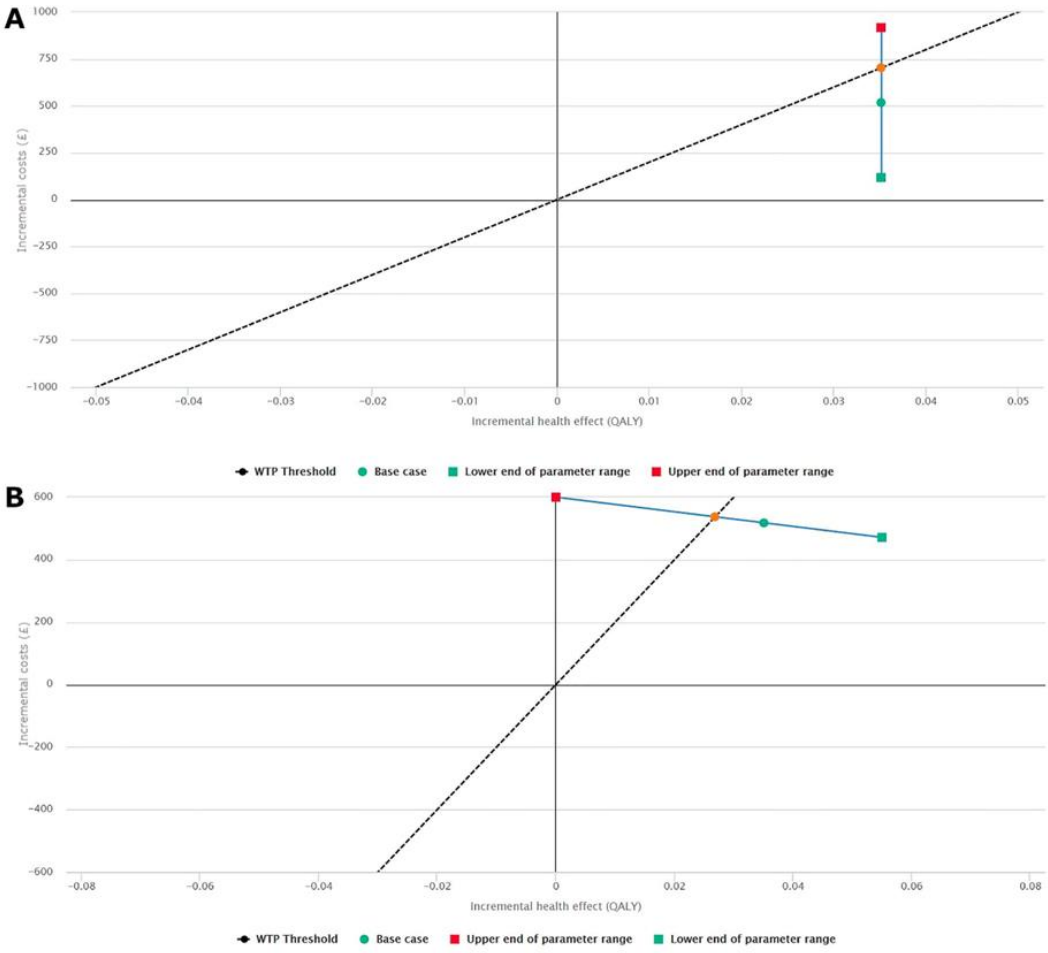


Fig. 7 Early stage HTA process (Payers).

12.1 Case Study: Early Cost Effectiveness Analysis of Electrochemotherapy as a Prospect Treatment Modality for Skin Melanoma

The increasing prevalence of advanced skin melanoma, particularly Stage IIIc/IV, presents a significant challenge for healthcare systems worldwide. Traditional treatment modalities often focus on palliative care, aiming to alleviate symptoms rather than cure the disease. With the advent of new therapeutic approaches, such as electrochemotherapy (ECT), it becomes imperative to evaluate their cost-effectiveness to determine their feasibility and value in resource-limited healthcare settings. Electrochemotherapy combines the administration of chemotherapeutic agents with electric pulses to enhance drug uptake by cancer cells. This innovative approach has shown promise in treating various cancers, including skin melanoma. However, its adoption in clinical practice requires rigorous cost-effectiveness analysis to ensure it offers value for money compared to existing standard treatments.

The standard care for advanced skin melanoma often includes palliative treatments aimed at symptom management rather than curative intent. These treatments, while essential for patient comfort, may not significantly extend survival or improve quality of life. In this context, electrochemotherapy's potential to offer better outcomes warrants thorough investigation.

We enrolled 23 patients with Stage IIIc/IV skin melanoma who were treated with electrochemotherapy at the Institute of Oncology in Ljubljana, Slovenia. The study design included the following key components:

Cost Calculation: We calculated treatment costs using patient-specific data, capturing all relevant expenses associated with electrochemotherapy and standard care.

Quality-Adjusted Life Years (QALYs): We estimated QALYs through the EQ-5D-3L questionnaires, which assess patients' health-related quality of life.

Markov Model (Fig. 8): We employed a discrete-time Markov model to estimate lifetime costs and outcomes for both treatment modalities. This model allowed us to project the long-term economic and health impacts of electrochemotherapy.

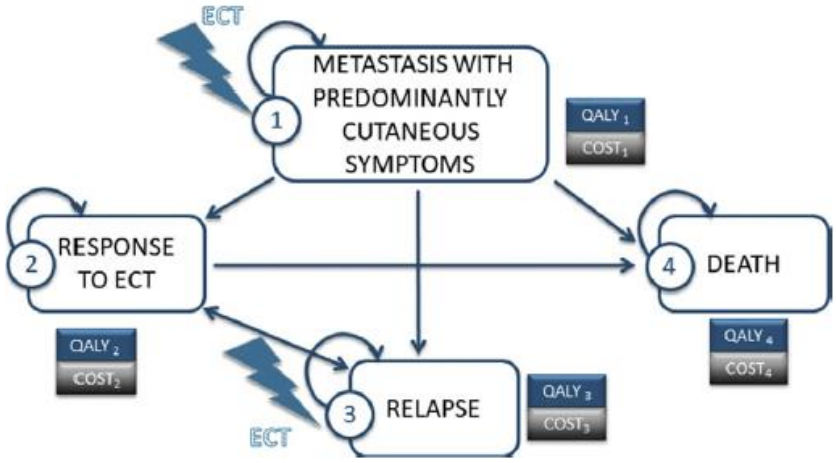


Fig 8 Markov Model.

Sensitivity Analyses: To ensure the robustness of our findings, we conducted sensitivity analyses, varying key parameters and assumptions to test their effects on cost-effectiveness outcomes.

Our findings reveal that electrochemotherapy increased QALYs by 0.29 at an additional cost of €6568 compared to the standard care. At a cost-effectiveness threshold of €20,000 per QALY, the probability of electrochemotherapy being cost-effective was 0.30 for the entire patient sample. Notably, for patients with bleeding lesions, this probability increased to 0.91. Moreover, reducing the price of electrodes by 50% could further increase the probability of cost-effectiveness to approximately 0.64 for the whole sample.

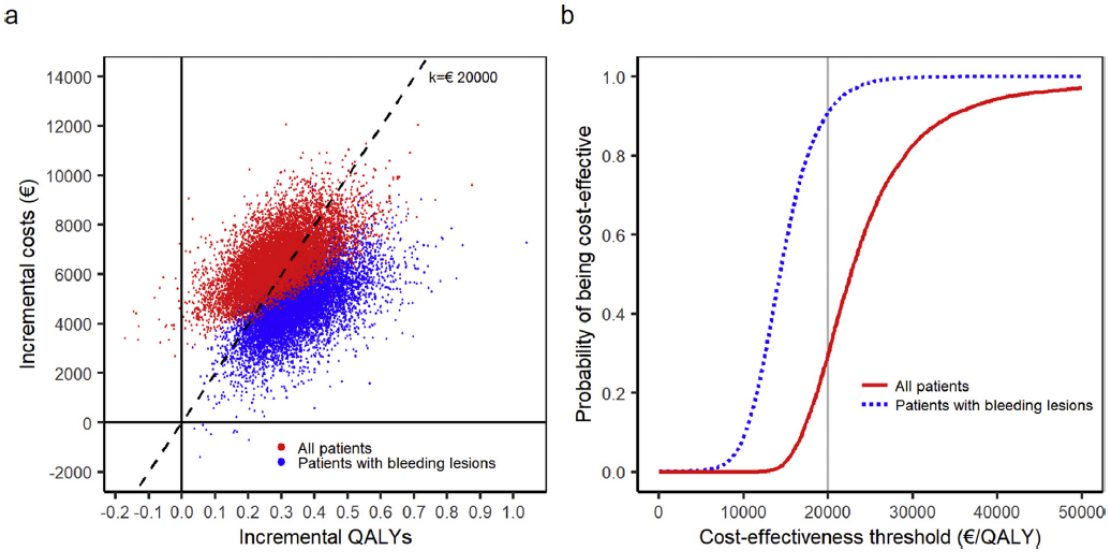


Fig. 9 (a) Incremental Cost-Effectiveness Plane, (b) Acceptability Curve.

These results indicate that while electrochemotherapy may be cost-effective for patients with bleeding lesions, the overall sample presents a more nuanced picture, highlighting the importance of context-specific evaluations.

12.2 eHTA in Fit4MedRob context

In the Fit4MedRob context similarly as Part I about HTA, eHTA will be conducted on device in early development based on the Technology Readiness Level (TRL) from 4 to 6. Tables developed for HTA in Part I, will be adopted as well for eHTA readapting based on the specific Medical Device to be analysed. So, methodology will be kept similar in the analysis, the main difference is in the source of the data as specified in section 10.4.

13. PART III BUSINESS MODELS

This part presents the most relevant tools and strategies for designing and implementing sustainable business models and plans for bringing developed and validated robotic rehab solutions into the market.

The condition that the rehab solutions alone (that is a system of robotic solutions only), or involved in mixed scenarios (traditional and robotic rehab training in inpatient, outpatient, and/or at home regimes) are sustainable from the clinical (i..e, the proposed solution is not inferior to the standard of care) and non-clinical perspectives, is the first condition for any future business plan aiming at suggesting strategies for a) obtaining positive revenues for the technology producers and sellers; b) satisfying the users and the payers.

The part is ideally divided into two connected issues: a) business models, chapters 14-16 and b) business plan for robotic rehab solutions (chapter 17).

14. INTRODUCTION

14.1 RELATIONSHIP BETWEEN EHTA, HTA AND BUSINESS MODELS AND PLANS

While the unwritten law of technology adoption and diffusion suggests that simply dominating the solutions that are available in the market is not enough for a technology to be adopted, in the healthcare sector, meeting the standard of care is essential for reimbursement. Reimbursement is critical for driving the adoption and diffusion of health technology. Consequently, the value of a proposed technology and its associated services must meet certain criteria dictated more by the standard of care than by its position on the technological frontier.

In the healthcare sector, demonstrating that a technology is not inferior to the standard is the necessary (though not sufficient) condition around which a business model and plan are constructed.

14.2 WHAT YOU CAN FIND IN THIS PART

Part III of the deliverable outlines the criteria, principles, tools, and procedures that will be employed to design business models and business plans for introducing new robotic rehabilitation technologies into the market and enhancing the diffusion of existing rehab robotic solutions. The prerequisite for being supported by a business model and plan is that these technologies must have demonstrated their cost-effectiveness through the adopted multilevel, multidimensional, and multi-stakeholder approach of Health Technology Assessment (HTA) (refer to Parts I and II).

14.3 DIFFERENCES BETWEEN BUSINESS MODELS AND BUSINESS PLANS

Part III is primarily dedicated to detailing how we will design business models and business plans for cost-effective robotic rehabilitation solutions. Therefore, providing a clear definition and description of the key distinctions between business models and business plans will enhance understanding of the nature and characteristics of the outcomes expected in the subsequent deliverables. Table 15 Compares definition, scope, purpose, flexibility and audience of business models and business plans.

Table 15 Business models and business plan, a comparison.

	Business model	**Business plan**
Definition	It describes how a company creates, delivers, and captures value, outlining the fundamental logic and structure of the business, including its value proposition, target customer segments, revenue streams, cost structure, and key activities.	It is a detailed document that outlines the goals, strategies, and operational details of a business. It typically includes sections on the company's executive summary, market analysis, marketing and sales strategies, organizational structure, financial projections, and implementation timeline.
Scope	To provide a high-level overview of how the business operates and generates value. It focuses on the core components that drive the business's revenue and profitability.	To provide a more detailed roadmap for achieving the company's objectives covering a wide range of areas, including market analysis, competitive positioning, marketing and sales tactics, operational plans, and financial forecasts.
Purpose	To define how the business will create and capture value. It helps entrepreneurs and stakeholders understand the fundamental drivers of the business and assess its viability.	To provide a comprehensive strategy and roadmap for launching or growing a business. It serves as a tool for securing funding, attracting investors or partners, and guiding the day-to-day operations of the business.
Flexibility	It can be relatively flexible and adaptable to changes in market conditions, customer preferences, or technological advancements.	Are more structured and detailed documents that may be less flexible to changes. They can be updated and revised over time but significant changes to the business plan may require substantial revisions and approvals.
Typical audience	Entrepreneurs, investors, partners, and other stakeholders interested in understanding the fundamental drivers of the business.	Investors, lenders, potential partners, and key stakeholders who require detailed information about the company's strategies, operations, and financial projections.

15. BUSINESS MODELS FROM AN INDUCTIVE PERSPECTIVE

15.1 METHODS AND PERSPECTIVE

15.1.1 Criteria for company selection

In order to collect data about companies in the rehab robotic market we followed a couple of steps which are here briefly described. The starting point was compiling a list of companies which operate in the manufacturing of the robotics solutions. We initiated from a company we already knew being active. The research about its offerings allowed us to collect information about other competing products, and hence of competing firms. We ended up with a list of 18 companies. The second stage involved collecting companies' data about: number of employees, year of establishment, country, type of management, entity (based on Dealroom taxonomy), value proposition, market target, market share (% based on value), partnerships, target markets, debt structure, total revenue, net income/loss, number of patents, and NACE code. All this data was collected browsing companies' websites and the Orbis database. All the information collected is presented in the tables in Appendix A.

15.1.2 Sentimental analysis

We conducted a sentimental analysis on the value propositions of the selected companies of EU, US, and APAC geographical areas. It consisted of the analysis of the frequencies of the words used by the companies to describe the added value of their solutions. The analysis has been conducted on those keywords with a minimum frequency equal to 4. Figure 3.1 reports the findings.

15.2 SUMMARY OF THE MAIN FINDINGS

15.2.1 Value proposition in EU, China e USA, sentimental analysis

There is an interesting difference among different geographic areas. A significant distinction lies in the use and detail of words adopted for describing the value proposition. EU and APAC companies tend to differentiate and strongly detail the nature and type of robotic rehab solutions, focusing on technology. When describing the value proposition, US companies prioritize addressing the problem and type of services, making them more service or solution oriented. These differences have significant implications for communication, acceptability, usability, and market orientation.

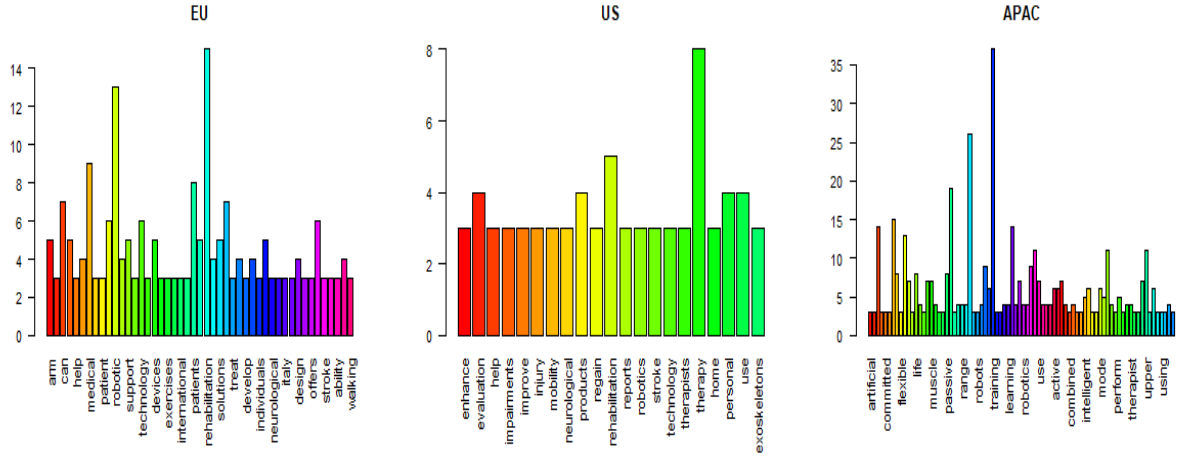


Fig. 10 Sentimental analysis of values proposition of UE, US, and APAC companies that produce robotic rehab solutions.

A technology-focused approach risks underestimating the importance of problem and solution complexity, the needs of end-users, and other stakeholders that should be assessed before developing new market-oriented technologies. Conversely, a market-focused solution may limit opportunities for radical innovations typically driven by curiosity and technology.

In general, basic research should be oriented towards curiosity-driven activities and efforts, while advanced research in the field of robotic rehab solutions should be more market-oriented (meaning considering user needs and the standard of care). However, currently, EU research and applications of robotic rehab solutions in clinical practice focus more on 'how' and 'what', rather than 'why'. This is why there is an urgent need for eHTA and HTA approaches. The techniques and models we have selected and developed will seek to answer: why use robotic solutions in rehab services? In this way, we do not miss the importance of the general purpose, which is not only to improve robotic rehab technologies or increase their diffusion but, firstly to prove that current rehab services may increase their effectiveness and sustainability thanks to robotic solutions. Diffusion will follow. The culture of eHTA and HTA will help ensure that the 'why' is not overlooked in the early and advanced stages of R&D.

15.2.2 The market

The current global market of rehabilitative robotics can be described as a high-risk one, in which large initial investments and high costs need to be sustained by companies to enter and survive. Ideally, only big companies feature the necessary financial resources to strive.

At the present stage, the main actors in this market are relatively young, medium-sized companies (more than 50 employees) and SMEs (less than 50), that produce an average turnover of about 17.5 million USD, which however is not sufficient to cover all costs. Not surprisingly, their results stand around an average yearly loss of 2.4 million USD.

Companies in this market are mainly located in the European Union, US, and APAC, are not family-owned and most of them rely on a B2B channel to sell their solutions to their customers, which are principally represented by both small/mid and large rehabilitative clinics and hospitals. In a few cases, however, companies also serve the B2C channel, supplying home versions of rehabilitation equipment to households, with the goal of offering the possibility to perform daily rehabilitation training independently at home. While direct sales are the first way by which business' products and services reach customers, a crucial role is also played by distributors and sales partners, which are vital to establish and enlarge companies' worldwide global presence. Target markets mainly include Europe and the Middle East, US and APAC.

Hospitals and clinics, together with universities, represent key business partners of rehab systems' manufacturers, indeed the latter can gain several benefits from such collaborations. Among others, companies can promote professional education, enlarge their R&D activity and leverage on synergies for the development of new solutions, conduct tests and research on their products/services with the possibility of either collecting data for the improvement of the device, and providing new and additional insights to research. In addition, participation in consortium projects has also been found to be an important gate to scientific knowledge, which is often embodied in several patent filings and used in R&D projects.

Based on the features presented above and considering the current Italian industrial fabric, it is possible to assert that the latter does not offer the ideal conditions to favor a fully integrated R&D, engineering and production of robotic rehab solutions. Large initial investments in R&D and specific devices to build the necessary know-how represent just the starting point of a longer journey. On the other hand, however, more profitable opportunities for market actors arise when the rehab solution is thought of and provided not only as a product per se, but as a service, which can be provided in conjunction with other facilitating services, such as tailored financial and consultancy ones. As a result, hence, the key of the Italian industrial fabric's competitive advantage stands in the integration of the research centers' activity with the competencies and skills of those small but highly specialized product engineering companies, an integrated system which can enable a strong and sustainable development of the rehab robotic industry in the Italian industrial context.

16. TOWARD A BUSINESS MODEL CANVAS BMC

16.1 STRUCTURE AND ISSUES OF A BUSINESS MODEL CANVAS FOR ROBOTIC REHAB SOLUTIONS

The design of a business model canvas for rehab robotic solutions will heavily rely on the market position and the company's standing within the related supply chain.

The rehab robotic solutions supply chain, which describes how materials, resources, information, services flow from their original sources to final consumers, encompasses different activities which can be performed by only one or more firms, depending on the degree of vertical integration of the organizations operating in the industry. As depicted in Figure 5, the main stages concern R&D, production, distribution, marketing & sales, customers, and after-sale services.

The following paragraphs present the business model of a vertically integrated manufacturing company, in which all activities, starting from R&D to the after-sale services are performed in-house or in collaboration with other organizations. As stated, however, it is important to underline that this is not the only one solution, given that many other business model opportunities can arise along the supply chain. As an instance, we could take the perspective of a research center or an university, which business model if focused on the R&D activity, or of a distributor, which is focused on reaching customers, selling the rehab solution and managing the after-sale service, or of a rehabilitation center (hospital or clinic) which uses the assistive device to improve its rehab treatments. The perspective of the latter - adopters - will be addressed in the following deliverable, even though it is already integrated in the Part I HTA of this deliverable.

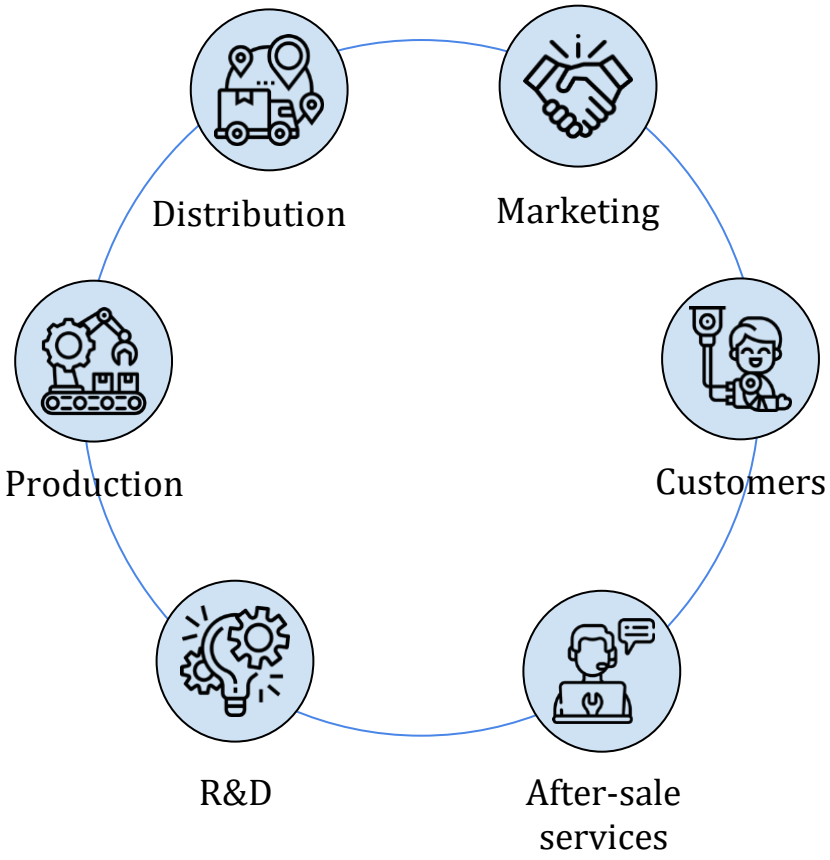


Fig. 11 The rehab robotic solutions supply chain.

The business model of an organization can be defined as the logical schema that shows how it works to reach its goals, may they be profitability, growth, or generating a social impact. At the moment there's no agreed-upon definition of business model, however we can recall the definition given by Osterwalder & Pigneur (2010) in their book: "A business model describes the rationale of how an organization creates, delivers, and captures value", and the more comprehensive one given by Fielt (2013) "A business model describes the value logic of an organization in terms of how it creates and captures customer value and can be concisely represented by an interrelated set of elements that address the customer, value proposition, organizational architecture and economics dimensions". It is this second definition that allows us to introduce the concept of Business Model Canvas, a logical schema and a shared language to describe, visualize, assess and change the business model of a firm (Osterwalder & Pigneur, 2010). Figure 12 depicts the Business Model Canvas made up of the nine building blocks, together with the links among them.

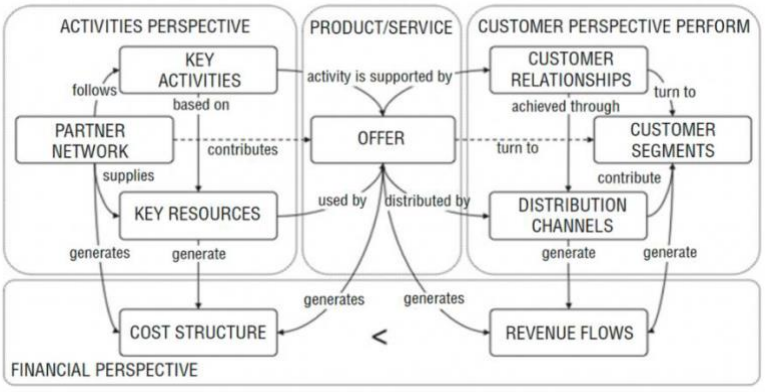


Fig. 12 The Business Model Canvas.

The nine building blocks of the Business Model Canvas are grouped into four pillars, namely customer perspective, product/service, infrastructure management or activities perspective, and financial perspective, which are briefly described here.

The **Value Proposition** building block corresponds to the product/service pillar, which function is to describe WHAT a company offers, to the market to solve customers' problems or to satisfy their needs. It can be intended as an aggregate of benefits that organizations create for their customers, which may be radically new, or similar to other devices already existing in the market. The value proposition of companies in the rehab robotics market can be described as solutions (see sections 15.1.2, 15.2.1), which are developed and offered to customers to ultimately improve the quality of life of their patients. When talking about benefits, however, a distinction has to be made between benefits accruing to clinics and hospitals, in which operators use the device in order to perform the rehabilitation treatment, and benefits accruing to patients, who receive the treatment. Benefits accruing to **clinics** and **hospitals** include the possibility of:

- improving and relieving the work of specialists (for example, active participation in repetitive hand exercise is important for stroke rehabilitation training: the rehab robot can provide the patient with repetition of movement, without making the therapist overly fatigued);
- having more effective results, generating a positive impact on patients' morale and motivation;
- collecting clinical data about therapy that allows both to evaluate and report about a patient's progress, and enable the most effective treatment plan;
- treating and challenging patients in a controlled environment;
- setting group training sessions, improving efficiency.

Patients' benefits include instead the possibility of:

- performing therapy in an innovative way by performing motivating exercises, while restoring motor function and regaining mobility;
- keeping motivation high, a key element for a successful rehabilitation;
- obtaining enhanced outcomes, paving the way for functional recovery;
- increasing therapist focus on the patient;
- (in certain cases) continuing therapy at home;
- improving independence, quality of life and mental health.

Customer Segments, Channels, and Customer Relationships blocks constitute the second pillar of the canvas, namely the customer perspective, which specifies TO WHOM companies create value, how they are reached and how the relationship with them is maintained.

The **Customer Segments** element determines for whom the organization is creating value and who the most important customers are. It includes, indeed, both groups of people and/or organizations that the company decides to reach and serve, having a clear and strong understanding of their needs, based on which the entire business model is shaped. In the case of rehab robotic providers, customer segments typically consist of **rehabilitation centers**, such as **hospitals** and **clinics**, that want to rethink rehabilitation with technology advanced assistive devices, as well as patients that are the ultimate beneficiaries of the technology. The final goal that drives the adoption of robotic rehab devices includes the willingness to improve independence and quality of life of patients.

The **Channels** building block creates the points of contact between Customer Segments and the Value Proposition and it includes all the interfaces on which companies rely to reach their customers. In particular, rehab robotic companies mainly rely on two major distribution channels, namely **direct sales** and **distributors**, which allow them to be present either locally, where their own branches are based, and globally. Companies' network of distributors play indeed a key role in making products available worldwide.

Customer Relationships block, which links Customer Segments and Value Proposition alike, includes the type of relationships organizations institute with customers, which can span from personal connections to automated ones. The choice of one kind or another is dictated by the goal the organization has, such as acquiring new customers, holding them, or boosting sales. Generally, companies in the assistive robotics sector offer personal assistance to their clients, through dedicated **after-sale teams** and **distributors**. Personal connection in this field is crucial to ensure customer assistance and satisfaction.

Moving to the left side of the Business Model Canvas, the Key Resources, Key Activities, and Key Partners building blocks make up the infrastructure management or activities perspective pillar, which describe HOW the company is able to acquire the necessary inputs and operate to produce the Value Proposition. In detail, the **Key Partnerships** element contains the set of relations the business has with its suppliers and other partners. Key partners of rehab robotic companies include **universities** and **research centers**, that on one hand provide access to scientific knowledge with a view to developing and launching new products, and on the other they can advance fundamental and applied research based on the most advanced devices present in the market. **Hospitals** and **clinics** are key partners too, allowing companies to introduce and test their devices in increasingly new settings, and gather feedback from operators. Finally, strategic collaborations with **other bigger companies** need to be mentioned too, given the possibilities for organizations to leverage on the strengths of the two, such as having access to additional financial resources to invest and expand R&D, to support the manufacturing process, giving assistance in the marketing of the product in foreign markets, etc.

The **Key Resources** block contains the assets the organization may own, lease or acquire from key partners to conceive and produce the Value Proposition, bring it to the market, and earn revenues on it. In the rehab robotic sector, the **intellectual resources** are the most valuable, which can be embodied in the R&D activity performed by engineers, researchers and developers, and in the **patents** an organization may obtain, own or acquire. Owning or having access to a well-equipped R&D center is also a crucial element for a successful development of high-tech devices. Among key resources it is also necessary to mention the **manufacturing** and **marketing infrastructure** necessary to produce the products, eventually in mass, and bring them to market.

Similarly, the **Key Activities** building block describes the most important actions the firm must perform to operate, and therefore, to sustain the blocks on the right side of the canvas. As before, the most important activity concerns **R&D**, which is at the basis for new product development and for already existing products improvement. Providing an initial consultancy, training, pre- and post-sale assistance on device usage is also key for a successful introduction of the product in the rehabilitation setting. **Participation in consortium and projects** is another fundamental activity that grants organizations access to excellent scientific knowledge, other than allowing them to enrich their network. To conclude, other two key activities concern the manufacturing of the devices and their marketing, to either produce and sell the technology.

At the bottom of the Business Model Canvas, there are the Cost Structure and Revenue Streams blocks, which address the HOW MUCH question, hence the financial dimension of a business model. In particular, it refers to the aspects of the model that focus on how the business generates revenue, manages costs, and achieves profitability. The financial dimension of a business model is critical for ensuring the sustainability, profitability, and growth of the business. It provides a framework for understanding the financial aspects of the business and making informed decisions to achieve financial objectives.

The **Cost Structure** building block includes the most important costs that organizations have to sustain to operate the business model, which can readily be calculated after having defined the elements in the infrastructure management pillar. It includes both fixed costs (such as rent, salaries, and utilities) and variable costs (such as materials, production costs, and distribution expenses). Based on all the above, it is possible to assert that the most prominent cost items include those related to performing the **R&D activity** (researchers and engineers wages, costs of equipment, product prototyping, IP development and renewal, etc.), all the **manufacturing costs** (equipment, buildings, wages, raw materials, logistics, utilities, etc.) which can be lowered once the company is able to exploit economies of scale, as well as all the **selling and marketing costs** to bring the devices to local and foreign markets (these costs include for instance products registration costs in foreign countries).

The **Revenue Streams** block outlines the sources of revenue for the business, which depends on the revenue mechanism adopted by the organization. Revenue streams can be classified into two main categories: transaction revenues or one-time payments, when for instance the device is sold and readily paid, or recurring revenues generated by ongoing payments from renting or leasing the device or from the after-sale service.

Other elements related to the financial aspects of the business model include:

- **Profit Margins**: Profit margins indicate the difference between the revenue generated by the business and its total costs. This component of the financial dimension assesses the profitability of the business and determines the margin or percentage of revenue that translates into profits after accounting for costs.
- **Key Financial Metrics** used to evaluate the financial performance and health of the business such as gross margin, net profit margin, return on investment (ROI), cash flow, break-even point, etc.

- **Funding and Investment**: how the business secures funding and investment to support its operations, growth, and expansion plans (for instance sources of funding such as equity investment, debt financing, venture capital, angel investors, crowdfunding, or grants).
- **Financial Projections** forecast the business's future financial performance based on assumptions about revenue growth, cost trends, market conditions, and other factors.
- **Risk Management** identifies, assesses, and mitigates financial risks that may impact the business's financial stability and performance. This may include risks related to market volatility, regulatory changes, currency fluctuations, credit risk, or operational risks.

16.2 Business Model and the impact on financial statements

There are different ways in which a potential rehab robotic adopter (rehabilitation clinic, hospital, etc.) can introduce a device in its operations. Depending on the business model, the provider of a rehab robotic solution can sell, lease the device or adopt a pay-per-use model. The selling implies the traditional transaction-based business model, where there is the exchange of money on behalf of the property of the device. Leasing involves the possibility to use the device but without purchasing and having formally the property. The adopter is paying periodically an amount of money and only at the end of the contract, upon payment, could become the owner of the device. The pay-per-use model for a device fundamentally shifts the paradigm of ownership, offering businesses a flexible and cost-efficient alternative. In this model, rather than purchasing the device outright, companies pay only for the actual usage of the device.

Each of these three ways generate different costs and revenues impacting in different ways on the Balance sheet and Income Statement of the technology adopter and provider. The differences are briefly described in the following section.

The sale transaction entails that the rehab robotic adopter purchases the device from the rehab robotic provider. The sale is final, which means that the ownership of the device passes from the solution provider to the solution adopter once the latter obtains control of the asset and the provider acquires the right to consideration in exchange for the asset transferred.

Table 16 Sale: Impact on Financial Statements

Rehab robotic provider	**Rehab robotic adopter**
Considering the case in which rehab robotic solutions represent the core business of the firm, the sale of the device represents a source of revenue, which enters the Income Statement in the form of net sales and generates a cash inflow.	Once the sale takes place, the adopter becomes the owner of the asset, which enters the balance sheet as a long-term asset. The consequent financial effect is primarily a cash outflow. The cost of the device, as it will be used for many years, is capitalized and periodically depreciated impacting the Income Statement. (The periodic depreciation expense, which is recognized in the Income Statement, is calculated considering the historical cost, the salvage value, the eventual impairment loss, and the estimated useful life.)

The **leasing** implies a long-term contract in which the owner of the rehab robotic device (the lessor) allows the adopter (the lessee) to use the property for a certain period in exchange for a stated payment.

Financial leasing refers to a financing transaction, implemented by a bank or finance company, in which the lessor grants the user the use of the asset for a specified period of time in return for the payment of a periodic fee. The user assumes all risks related to the perishing of the asset and retains the option to purchase the asset at a predetermined price at the end of the contract. The customer, at the end of the contract, can in fact choose to return the asset or purchase it by paying the difference between what has already been paid and the price of the asset. Or, alternatively, he can decide to extend the term of the lease contract. In the financial leasing contract, the user must pay the lessor:

- A maxi initial fee
- Periodic payments of a fixed amount (which include interest to be paid to the lender)
- The final redemption price (usually less than the market value of the asset).

Operating lease refers to a financing transaction in which the lessor grants the user the use of the asset for a specified period in return for the payment of a periodic fee. These are often technological devices, machinery or office equipment, thus assets that are subject to rapid obsolescence and need to be replaced on a periodic basis. In the case of operating leases, the risk of obsolescence is placed on the supplier, which may coincide with the manufacturer itself or a third party, such as a bank. An operating lease is a contract that is not subject to a time limit, has no redemption option, and is not necessarily tripartite. In the case of operating leases, the user can decide, at any time and without notice, to terminate the contract or request replacement of the asset with a more modern one.

Table 17 Leasing: Impact on Financial Statements

Rehab robotic provider	**Rehab robotic adopter**
The rehab robotic provider, or the lessor, as owner, has the asset in the Balance Sheet as a long-term asset and will see a periodic cash inflow. Any related operating expenses will be represented in the income statement. In case of finance lease, the lessor recognizes in its Balance Sheet a lease receivable and a residual asset, reflecting the rights to receive lease payments and the residual value of the leased asset, respectively. In case of operating lease, the lessor continues to recognize the leased asset and records rental income over the lease term, reflecting the ongoing ownership of the asset and expectation of future economic benefits from it.	At the lease commencement date, the lessee (adopter) recognizes in its Balance Sheet the lease liability (equal to the present value of the lease payments) and a right-of-use asset. In a finance lease, two periodic expenses are recognized in the Income Statement: - the interest expense on the lease liability; - the periodic amortization of the right-of-use asset. If the lease classifies as operating, a single lease expense is recognized in each period, which comprises both the interest expense on the lease liability and the amortization of the right-of-use asset.

The **pay-per-use** model turns the rehab robotic device into a service, indeed through this method the rehab robotic adopter can finance the device as it benefits from it instead of purchasing it outright. The provider remains the owner of the device, which sells just the product's functionality, not the product per se. Usually price plans schemes are mainly two, **pay-per-use**, in which the provider charges a flat fee for a certain period, in addition to a usage rate for each use, and **pay-per-period**, or subscription schemes, in which a regular fee is charged regardless of usage.

Table 18 Pay-per-use: Impact on Financial Statements.

Rehab robotic provider	**Rehab robotic adopter**
The rehab robotic provider sells just the device functionality and charges the adopter based on usage (in a pay-per-use scheme). It is the owner of the device, so the long-term asset is in its Balance sheet, and therefore it is responsible for all investment and operating costs occurring during the life cycle of the product. A cash inflow measuring the revenues (in the Income Statement) from the use will be determined.	Also, in this case the adopter doesn't have to purchase the device but can just pay for the use of the asset. No investment or operating costs must be sustained, features that make this methodology a cheaper and more flexible option to the adopter of the technology. Costs in the Income Statement will be recognised related to the use of the device.

17. How to design a business plan for robotic rehabilitation

Designing sustainable business models for robotic rehab solutions is necessary but not sufficient to boost the production, adoption, and diffusion of these technologies in the healthcare sector. Designing robotic technology and service-specific business plans is mandatory for the companies involved in Fit4MedRob. This section introduces a general framework of business plans for robotic rehab solutions. Specific technologies and solutions developed and tested in Fit4Med will be referenced, and detailed business plans (along with related business models) will be provided in the updated version of the deliverable scheduled for the next year.

As reported in Figure 13 a business plan answers to three questions related to a product and/or a service:

1) To whom.
2) What.
3) How.

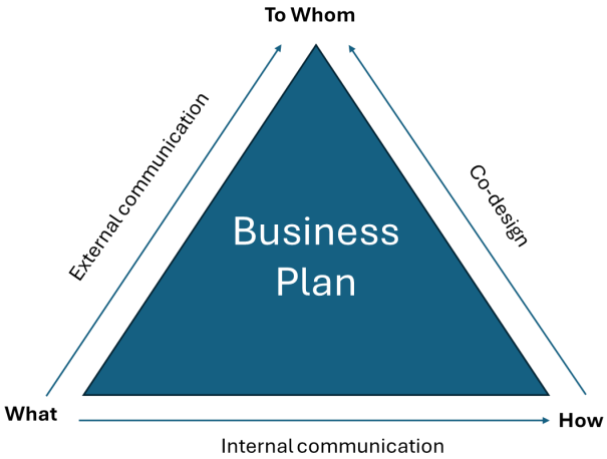


Fig.13 The macro-dimensions of a business plan

17.1 To whom? Market segmentation

Market segmentation for robotic rehabilitation and supporting solutions involves dividing the market into distinct groups of potential customers with similar needs, characteristics, and behaviors. Here are some key segments that correspond to some of the identified stakeholders.

- Clinical Settings

- Hospitals and Rehabilitation Centers: These facilities use robotic rehab technologies to provide therapy for patients recovering from injuries, surgeries, or neurological conditions. They require advanced robotic systems capable of delivering precise and customizable therapy sessions.

- Outpatient Clinics: rehabilitation services on an outpatient basis through compact, portable, and adaptable to various therapy settings robotic rehab solutions.

- At home use for people with disabilities or chronic conditions may use robotic rehab technologies at home for ongoing therapy and mobility assistance. At Home solutions are also viable answers for the aging population. As the population ages, there is a growing demand for home-based easy to use, safe, and able to address age-related mobility and strength issues robotic rehabilitation (but also supporting) solutions.

- Specialized Applications

- Neurological Rehabilitation: robotic rehab solutions (specialized devices for upper and lower limbs, and full-body) tailored for individuals with neurological conditions such as stroke, spinal cord injury, or traumatic brain injury.

- Orthopedic Rehabilitation for orthopedic conditions, such as joint replacement surgery or sports injuries, target improving range of motion, muscle strength, and functional mobility.

- Pediatric Rehabilitation necessary for children with disabilities or developmental delays.

- Therapeutic Focus

- Motor Rehabilitation: This segment includes robotic rehab technologies designed to improve motor function, muscle strength, and coordination. These solutions may target specific muscle groups or movement patterns and offer various assistive modes.

- Cognitive Rehabilitation: Cognitive rehabilitation focuses on improving cognitive abilities such as memory, attention, and executive function. Robotic rehab solutions in this segment may integrate virtual reality, gamification, and cognitive training exercises.

- Geographic Markets: that implies advanced and non-advanced healthcare infrastructure, different healthcare needs, budget constraints, and regulatory environments.

- Rehabilitation Professionals: physical therapists and occupational therapists play a key role in selecting and implementing robotic rehab technologies.

17.2 WHAT? PRODUCTS AND SERVICES

The definition of product and service characteristics should align with the elements of the marketing mix (product, price, promotion, place). All specific features and services should aim to overcome market barriers and outperform competitors.

17.2.1 Pricing strategies for robotic rehab technologies

Pricing strategies for robotic rehabilitation technologies can vary depending on factors such as market dynamics, competitive challenges, target customers, value proposition, and cost structure.

Below are some complementary/substitutive pricing strategies that robotic rehab producers and/or sellers should take into account in their business models.

- Cost-Plus Pricing: Once determined the cost of producing the robotic rehab technology, including development, manufacturing, marketing, and distribution costs, a markup is applied to cover desired profit margins. This approach ensures that all costs are covered and a profit is generated.

- Value-Based Pricing: the price is based on the perceived value of the robotic rehab technology to the customer, considering the benefits (for instance, improved patient outcomes, reduced rehabilitation time, increased patient satisfaction, and other relevant factors) it provides compared to traditional rehabilitation methods.

- Competitive Pricing: pricing strategies are supported by analysis strategies of competitors offering similar robotic rehab technologies.

- Penetration Pricing: the initial price of the robotic rehab technology is usually fixed lower than competitors' prices to quickly gain market share and establish a foothold in the market. This strategy can be effective for new entrants or when introducing innovative technologies to the market.

- Skimming Pricing: in the absence of competitors, it consists of fixing a high initial price for the robotic rehab technology to capture early adopters and customers willing to pay a premium for the latest innovation. The price is gradually reduced over time as competition increases or as production costs decrease.

- Bundle Pricing: it consists of offering the robotic rehab technology as part of a package or bundle with other products or services, such as rehabilitation services, training programs, maintenance contracts, or accessories. This can provide additional value to customers and justify higher overall prices.

- Subscription Pricing: the robotic rehab technology is offered on a subscription basis, where customers pay a recurring fee for access to the technology and related services. This can provide a predictable revenue stream, aligning pricing with ongoing usage or benefits received.

- Leasing or Rental Pricing: the robotic rehab technology is offered on a lease or rental basis, allowing healthcare organizations or final users to use the technology for a specified period in exchange for regular payments. This can reduce the cost barrier providing flexibility in usage.

- Segmented Pricing: it consists of tailored pricing strategies to different segments based on factors such as their willingness to pay, usage patterns, or specific needs.

- Government Reimbursement Pricing: In markets where government healthcare systems or insurance companies play a significant role, it should be necessary to align pricing with reimbursement rates or pricing regulations set by government agencies.

Experimentation, market research, and customer feedback will help companies involved in Fit4MedRob to refine pricing strategies over time to optimize profitability and market penetration.

17.2.2 Industrial design

Industrial design plays a critical role in creating robotic rehab technologies that are user-friendly, safe, aesthetically pleasing, adaptable, and reliable. By prioritizing user experience, safety, and innovation, industrial design contributes to the effectiveness and acceptance of robotic rehab technologies in clinical practice and rehabilitation settings. In this, industrial design is supported by the early assessment of acceptability and usability of robotic health technologies (see Part II devoted to robotic rehab eHTA).

17.2.3 Associated services (financial, B2B counseling and CRF solutions)

Robotic rehabilitation solutions are often accompanied by a range of associated services aimed at supporting users, clinicians, and healthcare facilities in maximizing the benefits of the technology. These associated services are essential for ensuring the successful implementation, adoption, and long-term use of robotic rehab solutions in clinical practice.

Training and Education: Comprehensive training and education programs offered to clinicians, therapists, and caregivers to ensure proper use and integration of robotic rehab technologies into therapy protocols (workshops, webinars, on-site training sessions, etc.).

Clinical Support and Consultation services: clinical support and consultation services to assist healthcare professionals in optimizing therapy programs, setting treatment goals, and interpreting patient progress data (clinical consultations, access to clinical experts, telehealth support, etc.).

Technical Support and Maintenance services: technical support services aiming at ensuring the proper functioning, maintenance, and troubleshooting of robotic rehab devices (assistance with hardware maintenance and software updates, calibration, and repairs, on-site maintenance visits and rapid response times for technical issues, etc.).

Outcome and reporting services: e.g, configuring outcome measurement protocols, generating progress reports, and benchmarking performance against peer institutions, helping clinicians to track patient progress, evaluate treatment effectiveness, and demonstrate outcomes to stakeholders. These services are often delivered through software platforms for collecting, analyzing, and reporting patient outcome data coming from robotic rehab solutions.

Customization and Integration services offer tools able to:

- customize and tailor robotic rehab solutions to the specific needs and preferences of individual users, clinics, or healthcare systems, therapy protocols, software interfaces;
- integrate robotic devices with existing electronic health record (EHR) systems.

Reimbursement and Financial Support services: guidance on coding and billing practices, reimbursement policies, and documentation requirements to maximize reimbursement for robotic rehab services, as well as financial assistance options about leasing, financing, or grant opportunities, etc.

Continuing Education and Research Collaboration services offering collaboration with academic institutions, research organizations, and industry partners to advance the field of robotic rehabilitation through research, development, and clinical trials. Continuing education programs and research collaborations enable clinicians to stay updated on the latest advancements in robotic rehab technology, also improving co-design and collaborations within research or industrial projects.

Patient Support and Engagement services that help users to maximize engagement and adherence to therapy programs: patient education materials, motivational coaching, progress tracking tools, and remote monitoring capabilities, also facilitating peer support networks or online communities for patients undergoing robotic rehab therapy, etc.

It is important to note that, under the hypothesis of the diffusion of robotic rehab solutions, each of the above-mentioned supporting services, as well as new ones, could be considered as separated potential businesses.

17.3 How? Internal strategies

17.3.1 Organizational structures

Designing and producing robotic rehabilitation (rehab) technologies necessitates a meticulously planned company structure that encompasses various functions and expertise. The organizational structure outlined below is applicable to a medium to large-sized company.

17.3.2 Executive Leadership

Chief Executive Officer (CEO): Provides the overarching strategic direction, leadership, and decision-making for the company. The CEO sets long-term vision and strategic objectives, ensuring all company activities align with these goals. Their ability to navigate market complexities and technological innovation is crucial for maintaining the company's competitiveness in the dynamic field of robotic rehabilitation.

Chief Operating Officer (COO): Oversees the day-to-day operations, including manufacturing, supply chain management, and quality assurance. The COO is responsible for operational efficiency, optimizing processes to maximize quality and productivity. They also manage operational teams to ensure that the finished products meet stringent industry regulations and customer expectations.

Chief Financial Officer (CFO): Manages financial planning, budgeting, accounting, and fundraising activities. The CFO plays a vital role in ensuring the financial health of the company, providing financial analyses that support strategic and operational decisions. They also monitor the company's financial performance, developing strategies to optimize costs and increase profitability.

17.3.3 Interaction and Synergy among Executive Leadership

Chief Executive Officer (CEO): The CEO acts as the central hub for the strategic alignment of all corporate activities. By maintaining a high-level view of the business landscape, the CEO facilitates cross-functional collaboration and ensures that company operations adapt to changing market demands and technological advancements. The CEO regularly interacts with other top executives to ensure that strategic initiatives are well-supported across the organization.

Chief Operating Officer (COO): The COO works closely with the CEO to implement the company's strategic vision in day-to-day operations. This role is critical for bridging the gap between high-level strategic plans and their operational execution. The COO coordinates with department heads to streamline processes, improve efficiency, and enhance product quality. They are instrumental in managing the operational logistics that underpin manufacturing and supply chain workflows, ensuring these align with the financial health and strategic goals overseen by the CFO.

Chief Financial Officer (CFO): The CFO provides the financial oversight necessary to support strategic decisions made by the CEO and operational implementations led by the COO. This includes financial risk management, investment decisions, and budget allocation that align with corporate strategies and market opportunities. The CFO ensures that financial resources are allocated efficiently, driving cost optimization without compromising on the innovation and quality standards set by the company's leadership.

17.3.4 Research and Development (R&D)

The Research and Development (R&D) department plays a pivotal role in driving the innovation and technological advancement of robotic rehabilitation devices. This section of the organizational structure is crucial for maintaining the company's competitive edge in a rapidly evolving industry.

Chief Technology Officer (CTO): The CTO leads the R&D department, setting the direction for research and development activities. This role involves a strategic oversight of the entire product development lifecycle—from conceptualization to design, testing, and implementation. The CTO ensures that technological innovations align with the company's strategic goals and market needs. By fostering an environment of creativity and technical excellence, the CTO encourages the exploration of new ideas and the integration of cutting-edge technologies into product designs.

Engineering Team:

The Engineering Team is composed of specialists in various fields:

> **Mechanical Engineers** develop the physical components of robotic systems, focusing on mechanics, dynamics, and materials suited for robust, efficient designs.

Electrical Engineers are responsible for the electrical control systems, wiring, and circuitry that power the robotics. Their work is crucial for ensuring the safety, reliability, and energy efficiency of the devices.

Software Developers create the software algorithms that control the robots, from basic movements to complex decision-making processes based on artificial intelligence and machine learning.

Biomedical Engineers bridge the gap between engineering and healthcare, ensuring that the robotic devices meet clinical needs and are safe for use with patients. They apply their understanding of biology and medicine to the design and enhancement of robotic systems.

Product Design Team: The Product Design Team focuses on the human aspects of the robotic rehab devices. This team plays a critical role in ensuring that the products are not only functional but also user-friendly, ergonomically designed, and aesthetically pleasing.

Key responsibilities include:

User-Centered Design: The team employs user-centered design principles to ensure that the devices meet the needs of both healthcare providers and patients. This involves extensive user research, usability testing, and iterative design processes.

Ergonomics and Aesthetics: Engineers and designers work together to ensure that the devices are comfortable to use and do not cause user fatigue or discomfort. The aesthetic aspects of the design also play a significant role in the marketability of the products, appealing to customer preferences and ensuring that the devices fit seamlessly into clinical environments.

The R&D department's success is measured not only by the innovation and technical excellence of the robotic rehab products but also by their practical applicability and market acceptance. Regular collaboration with the Regulatory Affairs, Clinical Affairs, and Marketing teams ensures that the products developed are compliant, clinically validated, and meet the market demands. This collaborative environment helps the company rapidly adapt to new scientific discoveries and technological advancements while ensuring that the products remain on the leading edge of the robotic rehabilitation field.

17.3.5 R&D Interaction and Collaboration

The Research and Development (R&D) department is the heart of innovation within the company, developing new technologies and improving existing products. Effective collaboration within this department and between R&D and other organizational units is crucial for fostering an environment that encourages creativity, problem-solving, and technical advancement. This section explores the specific interactions and collaborative practices that enhance the productivity and innovation capabilities of the R&D team.

Collaboration Within R&D Team: The R&D team comprises individuals from diverse technical backgrounds, including mechanical engineers, software developers, biomedical engineers, and more. The Chief Technology Officer (CTO) leads this team with a focus on fostering an interdisciplinary approach to project development. This includes:

- Regular Cross-disciplinary Meetings: Regularly scheduled meetings where team members share updates, brainstorm solutions, and discuss research progress help in aligning project goals and integrating various perspectives.
- Collaborative Workspaces: Physical and virtual spaces designed to encourage spontaneous discussions and idea exchanges among team members. These spaces are equipped with tools and technologies that facilitate collaboration and rapid prototyping.
- Joint Problem-Solving Sessions: Structured sessions that bring together diverse specialists to tackle specific technical challenges or innovation hurdles. These sessions often lead to breakthrough ideas and solutions that can significantly accelerate project timelines.

Interaction Between R&D and Operations: To ensure that innovations are not only theoretically sound but also manufacturable and marketable, R&D works closely with the Operations department. This collaboration is managed through:

- Integration Meetings: Regular meetings between the R&D leaders and Operations managers to discuss design practicalities and production capabilities. These meetings help to ensure that the designs are optimized for manufacturing from the early stages of development.
- Prototype Testing with Operations: Early and frequent testing of prototypes in a production-like environment to identify potential manufacturing issues or challenges.

- Feedback Loops: Establishing robust feedback channels through which the Operations team can provide real-time data and insights back to R&D, helping refine products and processes.

Linking R&D with Marketing and Regulatory Affairs: The R&D department also maintains strong collaborative ties with Marketing and Regulatory Affairs to ensure that product development aligns with market needs and complies with regulatory standards.

- Market-Driven Development: Regular updates and workshops with the Marketing team provide R&D with insights into customer needs and market trends, which guide the innovation process.
- Regulatory Guidance in Design: Continuous involvement of Regulatory Affairs in the R&D process ensures that all products are designed with compliance in mind from the outset, smoothing the path for regulatory approvals and reducing time-to-market.

17.3.6 Manufacturing and Operations

Vice President of Manufacturing: The VP of Manufacturing holds a critical role in overseeing the manufacturing operations, production planning, and quality control processes. This position is responsible for ensuring that manufacturing operations are efficient, cost-effective, and capable of producing high-quality robotic rehabilitation devices. The VP directs the entire manufacturing workflow, from raw material acquisition through final product assembly, ensuring that all products meet the stringent standards required in medical device manufacturing.

Production Team: The Production Team includes assembly workers, technicians, and manufacturing engineers who are directly involved in the hands-on building and testing of robotic rehab systems. This team works on the production floor to assemble parts into final products, conduct routine tests, and troubleshoot any issues that arise during the manufacturing process. Manufacturing engineers within the team also work to optimize production techniques and improve manufacturing processes, aiming to increase efficiency and reduce waste.

Supply Chain Management: The Supply Chain Management team is crucial for managing the flow of goods and materials needed for production. This includes negotiating and maintaining relationships with suppliers, managing procurement of components, and overseeing inventory management and logistics. Effective supply chain management ensures that the manufacturing process is not disrupted by shortages or delays in the supply of necessary components and helps control costs by finding the most efficient suppliers and logistics solutions.

17.3.7 Sales and Marketing

Chief Marketing Officer (CMO): The CMO is responsible for developing marketing strategies, brand positioning, and promotional campaigns to drive awareness and demand for the company's robotic rehab products. This role involves understanding market trends, customer needs, and competitive dynamics to effectively position the company's offerings. The CMO leads the marketing department in creating targeted advertising campaigns, managing digital marketing efforts, and organizing trade shows and public relations events to enhance brand visibility and product reach.

Sales Team: The Sales Team plays a pivotal role in the commercial success of the robotic rehab solutions. Team members are responsible for identifying potential customers, building relationships with healthcare providers, and driving sales. This involves direct outreach, presentations, and demonstrations of the robotic systems to hospitals, rehabilitation centers, and clinics. The Sales Team works closely with the Marketing department to convert leads generated by marketing efforts into actual sales, ensuring that potential customers understand the unique benefits and features of the products.

Customer Support and Training: This function is essential for maintaining customer satisfaction and loyalty after the sale. The Customer Support and Training team provides technical support, training, and after-sales service to customers, clinicians, and end-users. They ensure that customers can effectively use the robotic systems and benefit from all their features. Training programs are often conducted to educate users on the safe and effective use of the devices, and ongoing support is provided to address any operational issues or maintenance needs. This team plays a crucial role in building long-term relationships with customers and fostering positive experiences that lead to repeat business and referrals.

Each of these functions—Manufacturing and Operations, Sales and Marketing, Customer Support and Training—is integral to the overall success of the company. They ensure not only the production of high-quality and innovative products but also their successful introduction into the market and effective use by customers, thereby securing the company's position as a leader in the field of robotic rehabilitation.

17.3.8 Regulatory Affairs and Quality Assurance

Vice President of Regulatory Affairs: The VP of Regulatory Affairs plays a crucial role in navigating the complex regulatory landscape that governs medical devices. This executive is responsible for ensuring that all products comply with applicable regulatory requirements, such as those set by the FDA in the United States, as well as international standards where applicable. This involves leading the preparation and submission of documents required for regulatory approval and managing interactions with regulatory bodies. The VP of Regulatory Affairs also stays abreast of changes in regulatory policies and guidelines to anticipate shifts that might impact the company's product lines, thus ensuring continuous compliance and adapting regulatory strategies accordingly.

Quality Assurance Team: The Quality Assurance (QA) Team is tasked with maintaining the highest standards of quality and safety for all robotic rehabilitation technologies produced by the company. This team implements and oversees quality management systems that are compliant with both regulatory requirements and international quality standards, such as ISO 13485 for medical devices. They conduct rigorous testing and validation processes to ensure that every product meets the required specifications before it reaches the market. Furthermore, the QA Team continuously monitors product performance and safety through post-market surveillance, analyzing data from real-world use to identify potential improvements.

17.3.9 Clinical Scientific Affairs

Chief Medical Officer (CMO): The CMO provides vital medical expertise and clinical oversight within the company. This role involves guiding the development and validation of robotic rehab technologies to ensure they meet clinical needs and are supported by sound medical principles. The CMO works closely with the R&D and Regulatory Affairs teams to align product development with clinical expectations and regulatory requirements. This ensures that the products not only offer therapeutic benefits but also uphold the highest standards of patient safety and efficacy.

Clinical Research Team: The Clinical Research Team, under the leadership of the CMO, is responsible for conducting clinical trials and scientific studies that validate the effectiveness and safety of the company's robotic rehab solutions. This team designs and implements clinical studies, recruits study participants, and collects and analyzes data to assess the clinical impacts of the products. The results from these studies provide crucial evidence to support regulatory submissions and help in the marketing and commercialization of the products. The Clinical Research Team also collaborates with academic and research institutions to explore new applications for the technology and to stay at the forefront of advancements in rehabilitation science.

Together, these departments ensure that the company's products are not only innovative and technically proficient but are also clinically beneficial, safe for patients, and compliant with all regulatory standards. This comprehensive approach supports the company's mission to deliver high-quality, effective robotic rehabilitation solutions that improve patient outcomes and enhance quality of life.

17.3.10 Business Development and Partnership

Vice President of Business Development: The VP of Business Development is pivotal in driving the company's growth through strategic partnerships and collaborations. This role involves identifying and securing alliances with other companies, academic institutions, and industry leaders that can enhance the company's technological capabilities and market presence. The VP of Business Development evaluates and negotiates licensing opportunities, joint ventures, and co-development projects, aiming to expand market reach and access new technologies or markets. By forging these strategic relationships, the company can accelerate its growth and enhance its innovative capacity.

R&D Collaborations: A vital component of the company's innovation strategy involves establishing collaborations with academic and research organizations. These partnerships are crucial for advancing the state of technology and incorporating the latest scientific discoveries into the company's product development processes. Collaborations often result in co-development projects where academic insight and corporate practicality merge to create cutting-edge solutions. These relationships not only bolster the company's R&D capabilities but also enhance its credibility and standing in the scientific community.

17.3.11 Finance and Administration

Controller: The Controller is responsible for overseeing the financial reporting, analysis, and compliance of the company. This role ensures that all financial operations are conducted in accordance with accounting standards and regulatory requirements. The Controller prepares financial statements, manages audits, and plays a crucial role in financial

planning and risk management. By providing accurate and timely financial information, the Controller supports strategic decision-making and helps maintain the financial health of the company.

HR Manager: The HR Manager handles all aspects of human resources, including recruitment, employee relations, training, and benefits administration. This role is essential in maintaining a productive and engaged workforce. The HR Manager develops HR strategies that align with the company's overall objectives, oversees talent management processes, and ensures compliance with employment laws and regulations. Effective HR management contributes to a positive organizational culture and supports the company's ability to attract, develop, and retain top talent.

Administrative Staff: The Administrative Staff plays a crucial role in supporting various administrative tasks, office management, and the coordination of company operations. This group ensures the smooth functioning of day-to-day activities and supports other departments by handling logistical and clerical tasks. From managing office supplies to scheduling meetings and coordinating travel arrangements, the administrative staff helps maintain an organized and efficient work environment.

Together, these roles within Business Development, Finance, and Administration create a robust framework that supports the company's strategic goals and operational needs. By ensuring that the company operates efficiently, remains financially sound, and continues to grow through strategic partnerships, these departments are essential to the long-term success of the organization.

17.3.12 Cross-functional Collaboration for Innovation and Efficiency

The interconnection of various functions and responsibilities within an organization, whether through formal or informal channels, hierarchical or non-hierarchical structures, significantly influences the capacity for innovation and efficiency improvements. The organizational design, particularly in dynamic sectors like robotic rehabilitation, needs to be both flexible and structured to accommodate rapid changes and sustain growth. Depending on the size and scale of the operation, roles may be combined or expanded, and additional functions may be integrated to support specific business objectives. In companies, especially small and medium enterprises (SMEs), where production might be outsourced, it's crucial to maintain a hierarchical structure to ensure a well-organized division of labor. Conversely, R&D and other creative units benefit from a less hierarchical setup that fosters the cross-fertilization of ideas and promotes innovation.

Collaboration Between R&D and Operations: The Chief Technology Officer (CTO), leading the R&D team, works in close collaboration with the Chief Operating Officer (COO) and the Operations team to ensure that new technologies developed are not only innovative but also scalable and manufacturable. This partnership is critical for anticipating production challenges early in the design process. By integrating practical feedback from the operations team into the product development lifecycle, the company can reduce time-to-market and enhance the reliability and quality of the final products. Such collaboration ensures that innovative ideas are feasible in real-world application, bridging the gap between conception and practical deployment.

Collaboration Between Finance and Other Departments: The Chief Financial Officer (CFO) interacts extensively with all department heads, including those from R&D and Marketing, to ensure their fiscal plans are aligned with the overall company budgets and financial strategies. This role is pivotal in assessing the financial viability of new projects, forecasting returns on investment, and managing the capital necessary for sustained innovation and growth. Furthermore, the CFO is instrumental in developing pricing strategies with the Marketing department, balancing competitive pricing with profitability to ensure market success and financial sustainability.

Collaboration Between Regulatory Affairs and R&D: The Vice President of Regulatory Affairs ensures that all products adhere to global regulatory standards and manages the approval processes for new products. This role requires a close interaction with the R&D team to guide the development process within established regulatory frameworks, thereby minimizing the risk of compliance issues and facilitating smoother product launches. This collaborative effort is essential to ensure that innovations not only meet market needs but also comply with stringent regulatory standards, which is crucial for maintaining trust and safety in medical technologies.

17.3.13 Make or Buy strategies

Make or buy strategies in robotic rehabilitation refer to decisions regarding whether to develop (make) robotic rehab technologies and associated solutions in-house or to acquire (buy) them from external suppliers or vendors.

When deciding between make or buy strategies in robotic rehabilitation, organizations should consider factors such as their strategic goals, resources, capabilities, budget constraints, time-to-market requirements, and risk tolerance.

Hybrid approaches, such as strategic partnerships, joint ventures, or licensing agreements, may also be considered to leverage the benefits of both strategies while mitigating their respective challenges.

Table 19 Opportunities and challenges of make or buy strategies in robotic rehab R&D and engineering.

	Make	**Buy**
Advantages	▪ Full control over the development process, customization, and intellectual property. ▪ Flexibility and adaptation to specific needs, requirements, and technological advancements. ▪ Facilitates seamless integration with existing systems, workflows, and clinical protocols. ▪ It encourages innovation, R&D, and the development of proprietary technologies.	▪ Timesaving by leveraging existing solutions, technologies, and expertise. ▪ Lower upfront investment and reduced development costs compared to in-house development. ▪ Allows the organization to focus on core competencies, while outsourcing non-core activities. ▪ Transfers some risks associated with R&D, regulatory compliance, and market uncertainties to external subjects.
Challenges	▪ High costs. ▪ Time-consuming. ▪ It requires expertise in robotics, rehabilitation, software development, and regulatory compliance. ▪ Risks associated with R&D, e.g, technical challenges, regulatory hurdles, and market uncertainties.	▪ Reliance on external suppliers for technology, support, and updates, reducing control and flexibility. ▪ Transaction costs ▪ Ensuring compatibility, interoperability, and seamless integration with existing systems and workflows. ▪ Limited customization options may not fully meet the organization's specific needs or preferences. ▪ Potential limitations on intellectual property rights.

17.3.14. Requested personnel: necessary skills and competences

Key enabling technologies are IPs (patents that embody the necessary basic research) and the deep know-how and skills of engineers which are fundamental for the development of robotic devices. This issue also requires the definition of short and medium-time recruiting strategies and planning.

17.4 From What to Whom: External communication

Effective external communication is not only pivotal but also foundational for the successful adoption, integration, and market acceptance of robotic rehabilitation technologies. It forms the bridge between technological innovation and stakeholder engagement, ensuring that the benefits and applications of these advanced solutions are clearly understood and appreciated across a diverse spectrum of external parties. This chapter meticulously delineates the strategic approaches and methodologies employed to convey detailed and targeted information about robotic rehab technologies to various stakeholders including healthcare providers, regulatory bodies, potential investors, and the broader public.

The essence of these communication strategies is to articulate the unique value propositions of the robotic rehabilitation technologies, addressing specific concerns and interests of each stakeholder group. By deploying a range of tailored communication tools and channels, the aim is to facilitate a transparent, informative, and engaging dialogue that promotes the technologies' clinical benefits, operational efficiencies, compliance with healthcare regulations, and potential for investment returns.

Furthermore, external communication is intricately linked with the company's broader strategic goals—particularly in terms of market penetration, regulatory compliance, and community impact. External communication is a critical component in the lifecycle of product development and deployment, with an important role in overcoming market

barriers, facilitating smoother regulatory approvals, and ultimately driving the widespread adoption and sustainable implementation of robotic rehabilitation technologies in healthcare settings.

17.4.1 Objective and Strategy of External Communication

The primary objective of external communication in the context of robotic rehabilitation technologies is to create awareness, foster understanding, and build trust among key external stakeholders. The overarching strategy is designed to facilitate the diffusion of innovation by clearly articulating the scientific, clinical, and economic merits of robotic rehab technologies. This strategy serves multiple objectives:

1. **Enhance Visibility and Awareness**: Ensuring that stakeholders are not only aware of the new technologies but also to understand the potential impact on healthcare outcomes. This includes detailing the innovations brought about by robotic rehabilitation technologies and their benefits over traditional rehabilitation methods.
2. **Build and Maintain Trust:** Establishing a foundation of trust through transparent and consistent communication about the product's effectiveness, safety, and compliance with industry standards. Trust is particularly crucial when dealing with medical technologies, where stakeholder confidence can significantly influence adoption rates.
3. **Facilitate Market Adoption:** Communicating the value and utility of the technologies to accelerate their acceptance and integration into existing healthcare systems. This involves demonstrating economic value, ease of integration, and the support available to implement these solutions effectively.
4. **Support Regulatory Approval Processes:** Ensuring that all communications are aligned with regulatory requirements and contribute to a smooth approval process. This includes providing comprehensive data and clear evidence of compliance and safety to regulatory bodies.
5. **Attract Investment and Funding:** Communicating the business potential and prospects of robotic rehabilitation technologies to attract investors and secure funding. This involves highlighting market opportunities, potential returns on investment, and the strategic direction of the company.

Strategic Approaches

Segmentation and Targeting: Identifying and segmenting stakeholders based on their influence, needs, and roles within the healthcare ecosystem. Tailored messages are crafted to address the specific concerns and interests of each segment, such as clinical improvements for healthcare providers, return on investment for investors, and safety and efficacy for regulatory bodies.
Integrated Communication Channels: Utilizing a mix of traditional and digital media to ensure comprehensive coverage and reach. This includes professional journals, conferences, social media, webinars, and direct engagements through workshops and seminars.
Message Consistency and Compliance: Maintaining consistency in messaging across all platforms and communications to reinforce reliability and trustworthiness. Ensuring that all communications adhere to regulatory guidelines and ethical standards is paramount.
Feedback Mechanisms: Implementing mechanisms to capture feedback from stakeholders, which can inform ongoing communication strategies and product development. This includes surveys, feedback forms, and engagement metrics that help measure the effectiveness of communication efforts.
Crisis Communication: Preparing for potential communication crises by developing protocols to address and mitigate any negative publicity or misinformation effectively. This proactive approach helps in managing stakeholder expectations and maintaining the company's reputation in adverse situations.

Target Audiences and Messaging

Healthcare Providers:

- **Message**: Emphasis on clinical benefits, patient outcomes, and integration into existing therapeutic practices.
- **Channels**: Medical journals, conferences, webinars, and direct presentations.

Regulatory Bodies:

- **Message**: Focus on safety, efficacy, and compliance with medical standards and regulations.
- **Channels**: Regulatory submission documents, compliance reports, and formal meetings.

Investors and Partners:

- **Message**: Highlight the market potential, return on investment, and technological edge of the products.
- **Channels**: Business presentations, financial reports, investor meetings, and industry expos.

Patients and the Public:

- **Message**: Information on how these technologies can improve quality of life, ease of use, and accessibility.
- **Channels**: Social media, patient forums, community outreach programs, and patient advocacy groups.

Communication Tools and Materials

Brochures and Flyers: Provide succinct, accessible information about the technology, easily distributed at conferences or in clinics.
White Papers and Case Studies: Offer in-depth analysis and data on the effectiveness and efficiency of the technology, aimed at healthcare professionals and industry experts.
Press Releases and Media Outreach: Used to reach a broader audience through news outlets, highlighting significant achievements, new product launches, or milestones.
Digital Content: Includes website updates, blog posts, and social media activity that keep stakeholders informed and engaged with ongoing developments.

17.4.2 Feedback and Engagement

Effective communication strategies hinge on robust feedback and engagement mechanisms that gauge stakeholder responses and adapt as necessary to maximize impact. By actively monitoring social media engagement, analyzing feedback from patient use, participating in professional forums, and conducting satisfaction surveys among healthcare providers, the company can understand how its messages about robotic rehabilitation technologies resonate with different audiences.

Social media analytics offer real-time insights into public interest and sentiment, allowing the company to measure the reach and reception of its messages broadly. Feedback from patients, collected through digital forms, app analytics, and interviews, provides valuable information on user satisfaction and usability. Discussions in professional forums and conferences add a technical layer of feedback, focusing on the product's clinical integration and performance from the perspective of healthcare professionals. Regular surveys help the company assess healthcare provider satisfaction and the practicality of technology integration into clinical workflows.

To enhance feedback collection, the company incentivizes survey participation and employs real-time feedback tools on digital platforms, enabling users to report experiences and issues immediately. Longitudinal studies further enrich understanding by tracking user satisfaction over extended periods, offering insights into long-term impacts and sustainability.

17.4.3 Compliance and Consistency

Maintaining compliance and consistency across all external communications ensures the credibility and reliability of information shared about robotic rehabilitation technologies. This adherence involves strict observance of healthcare regulations, such as FDA guidelines in the U.S. or EMA standards in Europe, and alignment with corporate communication policies that dictate the content, tone, and style of messages.

The communications team undergoes regular training to stay updated on regulatory changes and corporate standards. This training is crucial for ensuring all communications are not only consistent with the company’s brand voice but also meet high ethical standards. A rigorous message review and approval process is implemented to ensure accuracy and compliance, involving legal scrutiny and technical verification by subject matter experts.

Documentation and diligent record-keeping of communications and supporting data are maintained for regulatory compliance and internal audits. Additionally, well-prepared crisis communication protocols are in place to manage potential miscommunications or public relations issues effectively, ensuring any misinformation is promptly corrected and stakeholder concerns are transparently addressed.

Through these meticulous practices in feedback, engagement, compliance, and consistency, the company ensures that its communication strategy robustly supports the strategic deployment of robotic rehabilitation technologies, facilitating widespread adoption while maintaining trust and integrity in every stakeholder interaction.

17.5 From How to What: Internal communication

Internal communication within the realm of robotic rehabilitation technologies is not merely a function of management; it is a critical component that shapes the organizational culture and drives the unified efforts of the team towards common objectives. Given the complexity and rapid evolution in the field of medical technology, maintaining clear and continuous communication channels across the organization is essential. This chapter delves into the nuanced strategies and innovative methods employed to facilitate robust internal communication, ensuring that all departments from engineering to sales, and from regulatory compliance to customer support, operate in synchrony. The effectiveness of these communications directly influences the organization's agility, its ability to respond to market changes, and its capacity for sustained innovation, ultimately enhancing overall organizational performance and boosting employee engagement.

17.5.1 Objective and Strategy of Internal Communication

The overarching objective of internal communication within the company is to cultivate an informed, engaged, and motivated workforce that is well-aligned with the company's mission and strategic goals. Effective internal communication fosters a sense of belonging and purpose among employees, making them feel integral to the company's success and well-informed about its trajectory. Key Strategic Aims Include:

- **Transparency**: Ensuring that information, whether about successes or setbacks, is shared openly across all levels of the organization. This transparency builds trust and helps to create an open culture where feedback is encouraged and valued.
- **Consistency**: Regularly delivering consistent messages through established channels to reinforce the company’s values and strategic objectives. Consistency in messaging helps to solidify understanding and reduce ambiguity, which is crucial in a high-tech environment where the stakes are high.
- **Clarity**: Communicating in a clear, accessible language that can be understood by all, regardless of their technical expertise or role within the company. This involves breaking down complex information into manageable, relatable content that enhances comprehension and actionable insights.
- **Engagement**: Designing communication to be two-way, allowing employees to voice their ideas, concerns, and suggestions. Engagement strategies include interactive sessions, town halls, and digital platforms where dialogue is encouraged and facilitated.
- **Empowerment**: Providing employees with the information they need to understand their role in the larger context of the company's objectives, enabling them to take initiative and act decisively. Empowerment through communication involves not just sharing information but also explaining the 'why' behind decisions and strategies.

Implementation of Communication Strategy

To achieve these aims, the company employs a multi-faceted communication plan that includes digital tools, face-to-face meetings, and personalized messaging to address the diverse needs and preferences of its workforce. The plan prioritizes adaptability, allowing for the swift incorporation of feedback and the dynamic adjustment of strategies to address emerging needs and situations. This approach not only enhances the relevance and effectiveness of communications but also fosters a proactive culture where employees are ready to engage with challenges and changes constructively.

Communication Methods and Tools

- **Intranet Platforms**: A centralized digital intranet platform serves as a hub for all internal communications, providing employees with easy access to information about company news, updates, policies, and procedures. This platform also hosts forums for discussions and feedback, allowing for a two-way communication flow.
- **Regular Meetings and Briefings:** Scheduled regular meetings for different teams and departments ensure that all staff members are aware of ongoing projects and initiatives. These meetings also serve as opportunities for team members to share ideas, give updates, and discuss challenges in a collaborative environment.
- **Internal Newsletters**: A weekly or monthly newsletter can highlight key achievements, upcoming events, and spotlight significant contributions from various teams or individuals. Newsletters help keep the workforce informed about the company's activities and successes, fostering a sense of unity and pride in their work.
- **Training and Development Programs**: Ongoing training sessions not only help employees improve their skills but also ensure they are up to date with the latest industry standards and technologies. These programs are also a platform for communicating important changes and developments within the company or industry.
- **Feedback Mechanisms**: Encouraging open dialogue through regular feedback mechanisms allows employees to express concerns and suggest improvements. Tools such as surveys, suggestion boxes, and interactive Q&A sessions with leadership ensure that employees' voices are heard and considered.

Ensuring Effective Communication

- **Segmentation and Personalization**: Tailoring communication based on the roles and responsibilities of different groups within the company ensures that information is relevant and useful. By segmenting the audience, the company can address specific needs and ensure that all employees receive pertinent information without being overwhelmed by irrelevant details.
- **Clarity and Brevity**: Communications are crafted to be clear and concise to prevent misunderstandings and ensure messages are easily digestible. This is particularly important in a tech-driven environment where complex information needs to be simplified for general understanding.
- **Visual Communication Tools:** Utilizing visual aids such as infographics, videos, and presentations can help in explaining complex processes and data more effectively. Visual tools are especially useful in training modules and detailed project updates.
- **Cultural Sensitivity:** In a diverse workplace, communications are designed to be culturally sensitive, ensuring that they resonate with all employees regardless of their background. This consideration helps in maintaining an inclusive work environment.

17.6 From How to Whom: Co-design

The co-design process, especially in the complex field of robotic rehabilitation technologies, is carefully structured to unfold over several stages. Each stage is intentionally designed to maximize collaboration among stakeholders and foster innovation from multiple perspectives. This phased approach not only ensures that all voices are heard, but also allows for iterative refinement of ideas and solutions, making the development process both dynamic and responsive to the needs and feedback of all participants.

Stages of the Co-design Process

1. **Preparation and Alignment**: Before actual design work begins, it is crucial to establish a common understanding among all participants. This stage involves setting clear objectives, defining the scope of the project, and aligning the goals of diverse stakeholders. Workshops and initial meetings are held to discuss expectations, introduce the technological possibilities, and lay out the constraints and challenges of the project. This foundation is vital for building trust and ensuring that the project moves forward cohesively.
2. **Ideation and Conceptualization**: The ideation phase is where creativity comes to the forefront. Participants engage in brainstorming sessions, leveraging techniques such as design thinking, storyboarding, and scenario mapping to generate a wide range of ideas and solutions. This stage is highly interactive and often involves the use of visual aids and facilitative technologies to help articulate concepts and capture thoughts effectively. The goal is to come up with innovative approaches that incorporate the needs and desires expressed by all groups involved, particularly end-users.
3. **Prototyping and Iteration**: With a set of concepts in hand, the next step involves turning these ideas into tangible prototypes. These early models or prototypes are developed using rapid prototyping tools that allow for quick

adjustments and modifications based on feedback. This iterative process is crucial as it allows stakeholders to interact with physical or digital versions of the product, providing insights that can only be gained through direct engagement. Feedback from this stage leads to refinements and further iterations, which progressively align the product more closely with user needs and expectations.

4. **Testing and Validation**: Once prototypes have been refined through several iterations, the next phase involves more formal testing and validation. This may include controlled testing environments or pilot programs within actual clinical settings where the device's performance and usability can be assessed in real-world conditions. This stage is critical for ensuring that the product meets regulatory standards and achieves the desired outcomes for functionality, safety, and user satisfaction.
5. **Implementation and Scale-Up**: After successful testing and validation, the focus shifts to implementation and scaling up production. This stage involves detailed planning for manufacturing, distribution, and market introduction. It also includes training programs for end-users and ongoing support systems. The transition from prototype to a fully marketable product requires careful management to maintain the integrity and intent of the original design, which was collaboratively created.
6. **Evaluation and Continuous Improvement**: The final stage of the co-design process involves ongoing evaluation of the product once it is in use. Collecting continual feedback from end-users and other stakeholders allows the company to adjust and improve. This stage ensures the product remains relevant and continues to meet the needs of its users as both technology and healthcare landscapes evolve.

Each stage of the co-design process is interlinked, with the learnings from one phase informing the activities of the next, creating a cycle of continuous improvement. This structured yet flexible approach ensures that the development of robotic rehabilitation technologies through co-design not only meets the current needs of users but also adapts to future challenges and opportunities.

17.6.1 Philosophy and Principles of Co-design

The philosophy of co-design is rooted in the principles of participatory design—a methodological approach that values the active involvement of all stakeholders in the design process. In the context of robotic rehabilitation, this includes end-users (patients and clients), healthcare professionals (therapists, nurses), engineers (mechanical, electrical, software), and business strategists. This collaborative engagement is predicated on the belief that the most meaningful and impactful innovations arise from a thorough understanding and integration of the diverse perspectives and experiences of these stakeholders. Core Principles Driving Co-Design Include:

- **Inclusivity**: Co-design commits to including a wide array of voices and perspectives in the development process. This principle ensures that the solutions developed are accessible and applicable to a broad user base, including those who may have unique or previously unaddressed needs.
- **Transparency**: By fostering an open environment where decisions and design processes are visible to all participants, co-design promotes a greater understanding of and confidence in the end product. Transparency in this context helps demystify the technology, making it more approachable and acceptable to users.
- **Flexibility**: Traditional design processes often suffer from rigidity, making it difficult to incorporate changes once development is underway. Co-design, by contrast, is inherently flexible, allowing for iterative changes and adaptations based on real-time feedback from stakeholders. This adaptability is crucial in the fast-evolving field of technology where user needs, and technological capabilities can change rapidly.
- **Empowerment**: Co-design empowers participants by valuing their contributions and giving them a stake in the outcome. This empowerment fosters a deeper engagement with the technology and can lead to more enthusiastic advocacy and adoption of the final product.

Through these principles, co-design strives to create a design process that is not only more democratic but also more dynamic, responsive, and ultimately effective in producing robotic rehabilitation technologies that truly meet the needs of their users. By placing the experiences and insights of end-users and other stakeholders at the heart of the design process, co-design ensures that the technologies developed are not only innovative but also grounded in the practical realities of those who will use them daily.

17.6.2 Benefits of Co-design

Engaging in co-design within the development of robotic rehabilitation technologies provides profound advantages that extend beyond the immediate design process. One of the most significant benefits is enhanced user satisfaction. When products are developed with direct input from those who will use them—the end-users—there is a greater likelihood that the final product will meet their actual needs and preferences. This alignment significantly increases the likelihood of higher user satisfaction and better overall user experiences, as the products are tailored to address specific requirements and challenges identified by those who encounter them daily.

This user-centric approach also leads to increased adoption rates. Products that emerge from a co-design process are inherently more aligned with user expectations and the practical clinical requirements of healthcare settings. This alignment ensures that new technologies are quickly integrated and adopted within professional environments, as they clearly respond to the users' real-world needs and workflows.

Moreover, the co-design process naturally fosters innovation through the diversity of perspectives it incorporates. By bringing together individuals from various backgrounds, including healthcare professionals, engineers, and end-users, the pool of ideas and potential solutions significantly broadens. This diversity often sparks unique solutions that might not have emerged in a more homogeneous or traditional design setting. The collaborative nature of co-design allows for the exploration of ideas from multiple angles, increasing the likelihood of breakthrough innovations that push the boundaries of what is currently possible.

Additionally, co-design can lead to a reduced time to market. By involving a wide range of stakeholders early in the design process, potential issues are identified and addressed sooner, which helps to align the product closely with user needs from the beginning. This early alignment and continuous feedback loop throughout the design and development phases streamline the entire process, minimizing the need for extensive revisions and reducing delays that typically occur when products are developed in isolation from their end-users.

Together, these benefits of co-design not only enhance the quality and functionality of the products but also ensure that they are accepted and integrated into daily use more quickly and effectively. The co-design process, therefore, is not just about creating products; it's about crafting solutions that are innovative, deeply integrated with user needs, and primed for success in the competitive marketplace.

17.7 THE FINANCIAL STRUCTURE OF THE BUSINESS PLAN FOR ROBOTIC REHAB

The financial structure of a business plan for robotic rehab solutions would include specific financial projections and considerations tailored to the development, production, and commercialization of these technologies. The following dimensions should be taken into consideration.

Startup Costs and Initial Investment required to develop and launch robotic rehab solutions, including R&D expenses, prototype development, regulatory compliance costs, and initial marketing expenses.

Break down the startup costs into categories such as equipment, technology licensing fees, employee salaries, legal and regulatory fees, and marketing expenses.

Model of revenue streams generated from the sale or licensing of robotic rehab technologies and related products or services.

Cost Structure (fixed and variable costs) for developing, manufacturing, and distributing robotic rehab solutions, including costs related with materials and components, manufacturing labour, overhead expenses, marketing and sales expenses, and administrative costs.

Financial Projections and sensitivity analysis, including income, cash flow statements, and balance sheets, for the next 3-5 years based on market demand, pricing, production capacity, sales growth, and operating expenses.

Funding required to support the development, production, and commercialization of robotic rehab solutions. This also requires a) the identification of sources of funding (equity investment, grants, or strategic partnerships, etc.); b) the specification of how funds will be allocated to different activities and milestones (R&D, production scale-up, marketing, sales expansion, etc.).

Profitability and Return on Investment (ROI): a) to evaluate the potential profitability of the business by analysing projected revenues, costs, and margins; b) to calculate key financial metrics e.g, gross margin, net profit margin, return on investment; c) to compare these indicators with industry benchmarks and investor expectations.

Regulatory and Compliance Costs. It is mandatory to estimate the costs associated with obtaining regulatory approvals and compliance with industry standards and regulations for medical devices, also including expenses related to preclinical testing, clinical trials, regulatory submissions, and ongoing compliance activities.

Risk Management: a) to identify potential risks affecting the financial performance of the business (for instance market competition, technology risks, regulatory changes, etc.); b) to develop strategies to mitigate risks and plans to address unforeseen challenges.

18. CONCLUSIONS

The deliverable summarises the outcomes of the activity aimed at defining and describing general principles, models, and analytical dimensions of HTA and eHTA, and methods to develop sustainable business models and plans for the technologies that will be tested in Fit4MedRob. We have analysed in detailed the relevant perspectives and variables that will allow us to assess the effectiveness and cost-effectiveness of robotic rehabilitation solutions, considering both clinical and non-clinical dimensions, economic and organizational factors, as well as acceptability and usability. We also focused on the methodologies and approaches to follow in order to build successful and sustainable business strategies to bring these solutions to market, highlighting their reimbursement, acceptability, adoption, and diffusion dimensions/barriers/criticalities and approaches that could be implemented to cope with them.

The work done and presented in the current deliverable (the first of a series of three) - that benefited from the continuous interaction with engineers and clinicians, and colleagues with legal, regulatory and ethical competencies belonging to A4 -, represents a solid methodological base for all the empirical activity that has just started (with the submission of the protocols of the first clinical trials) and that will see its full implementation in the next semesters.

In the next months, together with the development of the empirical activities in collaboration with colleagues of M1, M2, M3, we will organise meetings, webinars, courses in order to transfer to all the partners of Fit4MedRob Initiative more and more details of the approaches, the methodologies, and the technical details of the dimensions related to HTA, eHTA and sustainable business models and plans.

LIST OF ABBREVIATIONS

AI	Artificial Intelligence
BIA	Budget Impact Analysis
CBA	Cost-Benefit Analysis
CEA	Cost-Effectiveness Analysis
CMA	Cost-Minimization Analysis
CUA	Cost-Utility Analysis
DTCP	Diagnostic and Therapeutic Care Pathways
eHTA	Early Health Technology Assessment
EMA	European Medicines Agency
FDA	Food and Drud Administration
HTA	Health Technology Assessment
ICER	Incremental Cost-Effectiveness Ratio
ICT	Information and Communication Technology
ICUR	Incremental Cost-Utility Ratio
KPI	Key Performance Indicator
QALY	Quality-Adjusted Life Year
RCT	Randomized Controlled Trial

SSSA	Scuola Superiore Sant'Anna
UCBM	Università Campus Bio-Medico
NHS	National Health Service
ROI	Return of Investment
SME	Small and Medium-sized Enterprises
PNC	Piano Nazionale Complementare
OSS	Operatore Socio-Sanitario (Health Care Assistant in Italian)
TRL	Technology Readiness Level
TP	Transition Probability
HC	Health Condition
HCQ	Health-Related Quality of Life
E(HC)	Expected Health Condition
NPV	Net Present Value
SOC	Standard of Care
WTP	Willingness to Pay
PSA	Probabilistic Sensitivity Analysis
DSA	Deterministic Sensitivity Analysis
R&D	Research and Development

REFERENCES

- Bakoyannis, G., Zhang, Y., & Yiannoutsos, C. T. (2019). Nonparametric inference for markov processes with missing absorbing state. Statistica sinica, 29(4), 2083–2104.
- Briggs, A., Claxton, K., & Sculpher, M. (2006). Decision modelling for health economic evaluation. Oxford University Press.
- Caro, J. J., Et al. (2005). Pharmacoeconomics analyses using discrete event simulation. Pharmacoeconomics, 23(4), 232-332.
- Caro, J. J., Et al. (2016). Discrete event simulation for health technology assessment. CRC Press.
- Cooper, W. W., Seiford, L. M., & Tone, K. (2007). Data envelopment analysis: A comprehensive text with models, applications, references and dea-solver software. Springer.
- Drummond, M. F., Schulpher, M. J., Torrance, G. W., O'brien, B. J., & Stoddart, G. L. (2005). Methods for the economic evaluation of healthcare programmes. Oxford University Press.
- Llorian, E. R., Waliji, L. A., Dragojlovic, N., Michaux, K. D., Et al. (2023). Frameworks for health technology assessment at an early stage of product development: A review and roadmap to guide applications. Value in health, 26(8), 1258-1269.
- Fasterholdt, I., Krahn, M., Kidholm, K., Yderstræde, K. B., & Pedersen, K. M. (2017). Review of early assessment models of innovative medical technologies. Health policy (Amsterdam, The Netherlands), 121(8), 870–879.
- Federici, C., & Pecchia, L. (2021). Early health technology assessment using the MAFEIP tool. A case study on a wearable device for fall prediction in elderly patients. Health technology, 11, 995–1002.
- Fielt, E. (2013). Conceptualising business models: definitions, frameworks and classifications. Journal of business models, 1(1), 85-105.
- Gray, A. M., Clarke, P. M., Wolstenholme, J. L., & Wordsworth, S. (2010). Applied methods of cost-effectiveness analysis in healthcare. Oxford University Press.
- Goodman, C. S. (2014). HTA 101: introduction to health technology assessment. National Library of Medicine (US).
- Ijzerman, M. J., Koffijberg, H., Fenwick, E., & Krahn, M. (2017). Emerging use of early health technology assessment in medical product development: A scoping review of the literature. Pharmacoeconomics, 35(7), 727-740. Https://doi.Org/10.1007/s40273-017-0509-1

- Mobinizadeh, M., Mohamadi, E., Arman, H., Nasiripour, A., Olyaeemanesh, A., & Mohamadi, S. (2021). Topic selection for health technology assessment: an approach combining multiple attribute decision making and decision rules. Medical journal of the islamic republic of iran, 35, 40. Https://doi.Org/10.47176/mjiri.35.40
- Osterwalder, A., & Pigneur, Y. (2010). Business model generation: A handbook for visionaries, game changers, and challengers (vol. 1). John Wiley & Sons.
- Otten, T. M., Grimm, S. E., Ramaekers, B., Et al. (2023). Comprehensive review of methods to assess uncertainty in health economic evaluations. Pharmacoeconomics, 41, 619–632.
- Pecchia, L., & Craven, M. P. (2013). Early stage health technology assessment (HTA) of biomedical devices. The MATCH experience. In M. Long (ed.), World congress on medical physics and biomedical engineering may 26-31, 2012, beijing, china (vol. 39, pp. 533-536). Springer.
- Peirce, C. S. (1878). How to make our ideas clear. Popular science monthly, 12, 286-302.
- Pirc, Eva, et al. "Early cost-effectiveness analysis of electrochemotherapy as a prospect treatment modality for skin melanoma." Clinical therapeutics 42.8 (2020): 1535-1548.
- Spiegelhalter, D. J., Myles, J. P., Jones, D. R., & Abrams, K. R. (2000). Bayesian methods in health technology assessment: A review. Health technology assessment, 4(38), 1-130.
- Tattar, P. N., & Vaman, H. (2014). The k-sample problem in a multi-state model and testing transition probability matrices. Lifetime data analysis, 20(3), 387–407.

APPENDIX A

Table A.1 Companies selected in the inductive approach for designing the business plan.

Company	Website	No. of employees	Year of establishment	Country	Type of management	Entities (taxonomy dealroom)
BIONIK LABORATORIES CORP.	https://bioniklabs.com/	13	2009	US	Non-family business	Startup
SIFSOF LLC.	https://sifsof.com	3	2005	US	Non-family business	Startup
SIYI INTELLIGENT TECHNOLOGY CO., LTD.	https://www.siyizn.com/EN.html	51-200	2017	China	Non-family business	Scaleup
SENSING FUTURE TECHNOLOGIES, LDA	https://sensingfuture.com/en/about-us/	7	2011	EU - Portugal	Non-family business	Startup
REHAB ROBOTICS COMPANY LTD.	https://www.rehab-robotics.com.hk/index.html	11-50	2010	China	Non-family business	Startup
GUANGZHOU YIKANG MEDICAL EQUIPMENT INDUSTRIAL CO., LTD.	https://www.yikangmedical.com/	200+	2000	China	Non-family business	Corporate
NEOFECT CO.,LTD.	https://www.neofect.com/us/	47	2010	Republic of Korea	Non-family business	Corporate
MOTEK MEDICAL B.V.	https://www.motekmedical.com	52	2006	EU - The Netherlands	Non-family business	Corporate
HOCOMA MEDICAL GMBH	https://www.hocoma.com	160	1996	Switzerland	Non-family business	Corporate
HIWIN TECHNOLOGIES CORP.	https://www.hiwin.tw	4.050	1989	Taiwan	Non-family business	Corporate
MOVENDO TECHNOLOGY S.R.L.	https://www.movendo.technology/	23	2003	EU - Italy	Non-family business	Corporate
EMAC S.R.L.	https://www.emac.it/riabilitazione/	3	2019	EU - Italy		Startup
HUMANWARE S.R.L.	https://www.hmw.it/en/	4	1994	EU - Italy	Non-family business	Startup
REWALK ROBOTICS LIMITED	https://golifeward.com/	108	2001	Israel	Non-family business	Scaleup/Corporate
EKSO BIONICS HOLDINGS, INC.	https://eksobionics.com	73	2005	US	Non-family business	Scaleup/Corporate
TYROMOTION GmbH	https://tyromotion.com/en/about-us/	72	2007	EU - Austria	Non-family business	Scaleup/Corporate
MEDIMEC INTERNATIONAL S.R.L.	https://www.medimec.it/content/azienda	28	1973	EU - Italy	Family business	Corporate
IUVO Srl	https://iuvo.company/	19	2015	EU - Italy	Non-family business	Startup

Table A.2 Value propositions of the selected firms.

Company	Value proposition
BIONIK LABORATORIES CORP.	Bionik Laboratories Corp. is a robotics company providing neurological functional recovery solutions to improve the quality of life of millions of people with functional or mobility impairments by combining artificial intelligence, innovative technology and data solutions to help individuals regain mobility, enhance autonomy, and regain self-esteem. The product portfolio includes three robots for rehabilitation following stroke and other neurological conditions and four products in varying stages of development. Products' features include: Robotic-assisted shoulder & elbow therapy for impairments from stroke, spinal cord injury, multiple sclerosis, parkinson's disease, cerebral palsy, and other neurological conditions or injuries. Arm-only, hand-only, and integrated arm-hand evaluation and therapy activities. Allows isolated hand-only evaluation & therapy for distal-only impairments. New and improved evaluation and robot utilization reporting system. User interface improvements provide therapists with greater task guidance and facilitation Cloud-connected data analytics to know the level at which therapists are using the technology. Reports about: evaluation and therapy Logs, utilization reports, robot outcome reports.
SIFSOF LLC.	SIFSOF offers its clients soft robotic rehabilitation pieces of equipment for personal and professional use, which can accelerate and facilitate the rehabilitation process. This robot-assisted therapy produces highly intensive upper limb training while reducing the physical burden on therapists and provides patients a continued therapy and assistance at home using simpler devices to achieve the goal of recovery. Products' features include: Home & clinic application; Affordable treatment compared to traditional therapy; User-friendly; Multiple training modes.
SIYI INTELLIGENT TECHNOLOGY CO., LTD.	Siyi Intelligence is a high-tech company specializing in the development of medical rehabilitation robots. It is the leader of software rehabilitation robots in China. It constantly creates high-end rehabilitation equipment for hospitals and families, and makes unremitting efforts to improve the quality of life of patients. The hand function rehabilitation robot adheres to the brand concept of "Regaining new life, Start first from hands" and is committed to helping patients with hand dysfunction recover self-care ability and improve the quality of life. It combines flexible robot technology and neuroscience, meets the rehabilitative needs of passive training, assistant training, and resistance training in the whole cycle and effectively helps the rehabilitation of various functions of the hand. The features of the device home-version include: - safe and comfortable: flexible pneumatic artificial muscle, imported custom soft fabric; - easy to operate: knob operation, one-handed operation training, no need to run the hospital, guarantee training time and accelerate the recovery process, operate on your own without the assistance of others, - humanized design: half-cut design, that can be worn alone; - cost-effective: medical grade equipment, consumer price; - professional rehab: used in hundreds of clinical hospitals nationwide The features of the soft external skeleton for lower limbs rehabilitation (China's first) are: - light weight (<3kg, concentrated in the waist) - flexible artificial muscle - tendon assist (no joint damage) - artificial intelligence algorithms - voice-controlled emergency stop - clinical application - wide range of applications
SENSING FUTURE TECHNOLOGIES, LDA	We apply our consolidated experience in robotics to perform remote medical procedures for diagnosis, clinical intervention, and as an assistive technology. The application of these systems can reduce the geographical barrier between doctor and patient with excellent results in teleconsultation or telediagnosis. Our portfolio includes technical capacity in the fields of sensors, robotics, medical device prototyping, support for medical certification, and software development. The prosthetic robotic arm: - replicates the human arm's degrees of freedom; - is controlled through the wheelchair and adaptable to all electric wheelchairs; - is safe for the user; - is a medical device class 1. Our users achieve a new sense of autonomy and an improvement in their quality of life. The robotic arm can help maximize their skills and decrease dependence on family members and caregivers.
REHAB ROBOTICS COMPANY LTD.	Rehab-Robotics is committed to developing the most innovative and advanced technology for rehabilitation. Combining advances in robotics and neuroscience, our products can speed up stroke rehabilitation progress and help patients regain hand mobility. The hand rehabilitation device is an award winning, state-of-the-art sEMG driven robotic hand rehabilitation device that combines advances in robotics and neuroscience to enable stroke survivors to restore movement to their paralyzed hands. The therapy device is intended for use in patients that require hand and forearm rehabilitation. Potential goals for its use could be: motor learning via interactive use of the biofeedback system; help initiation of voluntary muscle contraction and voluntary movement; maintain voluntary muscle contraction and voluntary movement; control of abnormal muscle activity.

GUANGZHOU YIKANG MEDICAL EQUIPMENT INDUSTRIAL CO., LTD.	The company, established in 2000, is now a mature medical rehabilitation equipment manufacturer, with nearly 24 years of experience that is leading the development of intelligent rehabilitation robotics. In addition to our groundbreaking work in intelligent rehabilitation robotics, our diverse product offerings encompass physical therapy, occupational therapy, treatment tables, and more. Example of products: The upper limb training & evaluation system uses an upper limb training digital model and algorithm engineering, combined with upper limb rehabilitation theory, to simulate human upper limb movement in real time. The device can perform passive movement, active movement, and combined active and passive movement of upper limbs in multiple dimensions. The device integrates rehabilitation evaluation, scene interaction, daily life activity simulation training, intelligent programming training, and personalized trajectory learning and training. It provides upper limb functional assessment and training for patients with grade 0-5 muscle strength dysfunction to speed up the recovery process. Features: Passive and active movement training: The device can realize passive movement and active movement of upper limbs in multiple dimensions. Patients can train without muscle strength at all. Trajectory learning mode: Learn and record up to 3 minutes of manipulation trajectory, drive patients to perform manipulation trajectory restoration therapy training, and conduct a large number of repetitive rehabilitation training for early patients to improve training efficiency. Diversified training modes: The device offers a variety of training modes to meet the needs of patients in various stages of rehabilitation training. Passive training mode: The therapist can set up to 60s of daily activities as the patient's training trajectory. The system drives the patient to perform repeated, continuous and stable manipulation trajectory restoration training according to the set movement trajectory and through games and giving certain sensory stimulation. Active and passive training mode: The therapist can adjust the guiding force of the robotic arm to each joint of the patient's upper limbs according to the patient's condition. At the same time, if the patient cannot actively participate in the training within 5 seconds, the system will automatically transform into a passive training mode to drive the patient to complete the training. Active training mode: The patient can drive the mechanical arm to move in any direction. The training mode includes single joint training and multi-joint training. Pre-set trajectories: The device includes commonly used trajectories for upper limb training and the trajectories of daily life movements for patients to quickly train. Strong safety protection: The device has independent spasm monitoring and two emergency stop buttons. The software system also monitors the limit of the range of motion of the robotic arm in real time during the activity to comprehensively protect the safety of patients. Automatic switch between left and right side: the device can automatically switch between the left and right sides, reducing cumbersome operation. It also has laser alignment to assist the therapist to align the appropriate exercise position. Automatic restoration: after the training is over, the user can click the automatic restore button to return to the initial position.
NEOFECT CO., LTD.	Our clinically proven neurorehabilitation devices maximize arm and hand use through fun and functional gameplay. The hand rehab device has been developed to improve the arm and hand performance of adult patients with stroke. It is designed to improve the range of motion, coordination, and timing of a patient in training games, using the patient 's hand as a controller. The device was designed with neuroplasticity in mind: training programs promote motor learning and brain reorganization to improve arm and hand function for adults rehabilitating from stroke. Sensor technology detects and records movement data: the high-tech rehab device measures movements of the forearm, wrist, and digits with accelerometer and bending sensors. It allows progressive upper extremity rehabilitation at home: it goes beyond traditional resistance bands and putty to create occupation-based hand exercises in an entertaining virtual reality environment.
MOTEK MEDICAL B.V.	Enabling you to carry out advanced human movement research and rehabilitation. With Motek's solutions, you can be confident in your aims to improve human performance. As the global leaders in virtual reality robotics, we provide you with 20 years of pioneering research through our advanced, innovative devices. Work with cutting-edge technology and integration to enhance your clinical or research setup and create engaging platforms with virtual and augmented reality. Versatile hardware solutions: we build adaptable devices that achieve the highest possible data quality and synchronization for your needs. With our integrated tools, you can reliably manage experimental parameters and quickly collect real-time feedback in virtual reality. Through real-time data collection and analysis, our advanced equipment and software are there to fuel your ambition. Our system range includes everything from advanced treadmills and balance platforms to sophisticated virtual environments and body weight support systems. All our products are interconnected through our own software platform, producing real-time feedback and progress reports. Our products have many application options, enabling flexible high-level human performance research and efficient clinical treatment in neurological and orthopedic rehabilitation, physical therapy, sports and psychology. Integrated Software: our integrated software platform interconnects all hardware devices to provide real-time feedback and progress reports during research and patient rehabilitation programs. While our hardware systems are the body that brings your research and treatment desires into reality, our software is the heart that brings it alive. No need for 3rd party packages. Our solutions offer you not only both real-time and offline data collection and gait analysis, but also the opportunity to create your very own protocols and applications.
HOCOMA MEDICAL GMBH	Hocoma is proud to be the world leader for rehabilitation solutions for human movement therapy across the entire continuum of rehabilitation cooperating with health organizations across the globe. It has set itself the objective of developing and manufacturing high-quality robotic and sensor-based therapy. Our products provide benefits for patients and therapists, and they stand for safety and user-friendliness. Our products fulfil the requirements of international norms and legislation in the field of medicine. For patients: numerous studies show that combining technologies with conventional therapy leads to better outcomes. Robotic and sensor-based therapy provide greater intensity and are more effective in motivating patients. Game-like exercises with robotic and sensor-based devices make training more fun. For professionals: robotic and sensor-based technology do all the hard work so you can treat more patients. You can treat patients who suffer from different pathologies no matter what phase of their affliction they're in. We help you integrate advanced technology into your daily routine at the clinic.

HIWIN TECHNOLOGIES CORP.	The company is a professional manufacturer of worldwide motion control and systematic technology. We are proud of being recognized by the industry for our innovative technology. The principle of providing our customers with greater value through technological advancements and enhanced global competition is the foundation of HIWIN's plan to be the leader in the hi-tech industry. Hiwin offers a wide range of robotic product lines based on its precision manufacturing and proficient motion control and system technology. With the philosophy of providing a better way of life for mankind, it has also committed to the medical industry to develop rehabilitation equipment, healthcare living equipment and surgical equipment. The medical robots are based on its core technology of precision motion control. They are developed to assist medical practitioners in repetitive tasks and ease their daily burden, including rehabilitation robot, surgical robotic arm. Our goal is to innovate from customer needs and participate in improving the quality of human life. The gait training equipment is an automatic training system that combines weight-bearing standing, repetitive stepping and gait training. By providing intensive intervention in the early stage, boosting blood circulation via repetitive exercise and facilitating lower extremities movement via neuroplasticity, it can encourage patients and enhance their motivation toward rehabilitation. The process of transferring patients from wheelchairs to the equipment is safe and efficient via the patient transfer system. It also relieves the burden of medical practitioners and caregivers. The device is also provided with an intelligent monitoring software that records training parameters of each session, which can be used by therapists to adjust their rehab programs. It can also monitor several systems at the same time so that a therapist can supervise several patients' conditions simultaneously. Hiwin's products are highly customized and have a cost advantage due to vertical integration.
MOVENDO TECHNOLOGY S.R.L.	Movendo Technology is a biomedical company with a solid reputation for applying state-of-the-art robotic technology to develop effective, user-friendly rehabilitation and diagnostic tools, aimed at improving the quality of patient treatment. It develops data-driven solutions and services for prevention and rehabilitation combining robotics, AI and machine learning. The rehabilitation systems are tailored to meet the needs of individuals, physiotherapists, and clinicians. The company's offerings include: - a robotic system for the rehabilitation and functional assessment of the lower limb and trunk motor system, allowing orthopedic, neurological, geriatric and sports medicine practitioners to assess and treat patients with both neurological conditions and injuries; - a robotic device for the rehabilitation and sensorimotor assessment of the lower limbs and trunk that allows users to perform assessments and exercises in both standing positions, with bipodalic or monopodalic support for precise weight-bearing control, and sitting position.
EMAC S.R.L.	EMAC is the exclusive distributor in Italy for: Movendo Technology, Techno Concept, TyroMotion, EksoBionics, Dessintey.
HUMANWARE S.R.L.	Humanware was created to improve people's quality of life through robotic medical devices that revolutionize medical therapy. We design and develop new solutions and technologies in the field of medicine and in particular rehabilitation in order to support the recovery of patients and assist the work of clinicians; in addition, by providing tools capable of offering reliable and measurable data on the recovery performance of individuals. A spin-off company of the Scuola Superiore Sant'Anna of Pisa, we are the perfect nexus between academia and business activities: we apply all new knowledge in the scientific world to design a better future. We believe in improving people's quality of life by applying the innovation of robotics to medical therapy. We design and develop medical devices and robots for neurological rehabilitation to achieve important motor recovery goals for individuals who have been affected by a stroke, head injury or who have undergone surgery. Through our devices, we have taken part in the robotic rehabilitation revolution in Italy as key leaders, offering dynamic and interactive exercises that aim at the gradual rehabilitation of the patient, through actions contextualized in a game-based and fun environment, with a precise measurement of performance that encourages the desire for improvement, typical of gamification. The company offers: - a robotic device for the rehabilitation of the upper limbs, indicated in the recovery of the arm after a stroke and for post-traumatic and cognitive functional recovery, - a bio-mechatronics system with an arm equipped with sensors developed to promote arm rehabilitation after surgery (shoulder surgery, for example), or after ischemia or a stroke.
REWALK ROBOTICS LIMITED	Delivering life-changing futures with pioneering innovation and industry leadership. Our mission at Lifeward is to relentlessly drive innovation to change the lives of individuals with physical limitations or disabilities. We are committed to delivering groundbreaking solutions that empower individuals to do what they love. As a global market leader in pioneering life-changing solutions, our portfolio features several innovative products. We will continue to be the driving force to elevate the standard of care in overcoming physical limitations and disabilities. Lifeward is the leading source of innovations that support healthcare professionals through groundbreaking rehabilitation solutions in delivering life-changing results for people with physical limitation or disability and helping individuals to achieve results they never thought possible. Our portfolio of proven solutions spans the continuum of care, delivering functional and health benefits in clinical settings as well as in the home and community. Lifeward supports clinicians and patients every step of the way to revolutionize what is possible in rehabilitation, recovery, and the pursuit of life's passions in the face of physical limitations or disability. Lifeward is your source for healthcare solutions that go beyond current standards of care to revolutionize what is possible – enabling you to pursue the life you love through improved functional and health outcomes in rehabilitation and daily life. Lifeward is your partner through the evaluation, trial, training process, reimbursement support and beyond, with dedicated care team members for each step of the way.

EKSO BIONICS HOLDINGS, INC.	Ekso Bionics uses exoskeleton technology to enhance natural abilities and improve quality of life. We are the leading exoskeleton company to offer technologies that help those with paralysis to stand up and walk, enhance worker capabilities globally, and provide research for the advancement of R&D projects intended to benefit U.S. defense capabilities. Our mission is to amplify human motion by enhancing strength, endurance, and mobility across medical and industrial applications with advanced robotics. At Ekso Bionics, we use our unique blend of clinical and engineering expertise to develop disruptive robotics for rehabilitation and personal use. Now, patients post stroke, brain injury or spinal cord injury and those affected by MS are able to utilize Ekso's exoskeletons in therapy to regain basic movements or even the ability to walk again. The wearer may experience an increase in range of motion and activation of muscles they had difficulty with before. Company's devices have been developed to improve patients' gait or get them back up to work on balance with the help of our robotic exoskeletons. Products' value: - enterprise: neuro-rehabilitation treatment via acute care, inpatient rehabilitation hospitals (IRFs), outpatient rehab facilities, & VA medical centers - personal: home and community use by individuals utilizing personal exoskeletons eksoWorks - industrial: overhead support in automotive, aerospace, commercial construction, renewable energy, logistics, general manufacturing, residential construction, and more
TYROMOTION GmbH	We develop revolutionary technology-based rehabilitation devices that put patients at the heart of rehabilitation. We are a leading manufacturer of technology-based therapeutic devices to improve independence and quality of life for people around the globe. We utilize an evidence-based approach with all our devices, and patient improvement and positive outcomes is central to our technology offering. Active-assistive robotic technologies are intelligent devices that use sensors to monitor human movement and positioning, then use this feedback in order to interact with the patient. Combined with our software, our complete solution is designed to challenge and encourage you, using proven gamification techniques that provide the right mix of motivation and fun during rehabilitation. Tyromotion's offering consists in active-assistive robotic technologies for upper and lower extremities. All therapy devices are individually adaptable and give enough room to physicians and therapists to creatively tailor rehabilitation to each patient's specific needs. Products' goals include: - having more effective therapy time: let the technology do the hard and repetitive work for you. In group settings, patients train their neuroplasticity. - using patient-centered therapy: use precious one-to-one therapy sessions for patient-centered therapy approaches. Therapy is adaptable to each patient through therapy and assessment all in one system. - increasing your patients' motivation: benefit from increased patient motivation through gamification and by making progress visible. - benefitting from the right amount of intensity: patients need to be challenged but not over-burdened. Detailed assessments and data allow to individually optimize patient therapies.
MEDIMEC INTERNATIONAL S.R.L.	Helping children, adults and the elderly who have motor difficulties or cognitive disorders with innovative aids, so that they can increase their mobility, autonomy and quality of life. In Italy Medimec International imports and distributes products manufactured by the most qualified international companies. It can boast over fifty years of experience and a consolidated position in the rehabilitation aids market. Year after year Medimec Int. has grown, always offering the latest top quality products and technologically advanced systems, in addition to consulting and technical assistance. The company offers a gait trainer that has all the requirements to help users regain walking ability and thus regain daily autonomy. It was developed based on the numerous research findings in the field of motor learning, according to which intensity of therapy and frequent repetition of the exercise are the necessary factors for the rehabilitation of walking ability to be effective. The device is easy to use, with minimal preparation time and an intense training program to support each stage of motor recovery: regaining walking ability, increasing gait speed, improving endurance, and improving gait pattern. In addition, connectivity features allow all workout data to be sent directly to the therapist's smartphone or tablet, who can then evaluate it immediately or transfer it to the doctor.
IUVO Srl	Dedicated wearable robotic devices and exoskeleton solutions for various user and industrial needs. From invention to finalized products IUVO offers its services for the design and development of solutions based on analysis of specific applications. The medical exoskeleton is a powered active pelvis orthosis to support the gait of patients.

Table A.3 Strategies, market and financial results of the selected companies.

Company	Market target (B2B, B2C)	Partnerships	Target markets	Debt structure (USD)* *Last year available	Total revenue (USD)*	Net result (USD)*	Market share (% based on value)	# patents	NACE
BIONIK LABORATORIES CORP.	B2B	- Universities and research centers Massachusetts Institute of Technology (MIT) - Hospitals and clinics: Kindred Hospital Network - Other companies: Pro-Med Technology LTD - distribution agreement	US (~ 67% of devices installed) 20 countries worldwide (~ 33%)	Equity: -$1.640.588 (-49%) Debt: $5.002.715 (149%) * FY ended 31/03/2023	$1.805.000	-$4.946.000	0,306%	5 US patents granted 3 US patent applications pending	2660
SIFSOF LLC.	B2B Partially B2C		Asia Europe Middle East Africa Large portfolio of small/mid and large clients.		$90.000		0,015%		
SIYI INTELLIGENT TECHNOLOGY CO., LTD.	B2B & B2C	- Hospitals and clinics: More than 100 hospitals in the country Participation to Shanghai 2018 "Science and Technology Innovation Action Plan", science and technology support.	Over 80 countries 3,000 clinics 30,000 households					Rehab Robots have more than 20 patents	
SENSING FUTURE TECHNOLOGIES, LDA	B2B	Participation to National and European consortium projects. Member of the Clusters: - Ageing@Coimbra: regional consortium focused on active aging - Health Cluster Portugal: national cluster of all healthcare-related entities	32 countries (60% exported business volume)	Equity: $476.626 (56%) Debt: $377.666 (44%) * FY ended 31/12/2022	$503.839	$25.194	0,085%	15 R&D projects	6202
REHAB ROBOTICS COMPANY LTD.	B2B	- Universities and research centers: Hong Kong Polytechnic University - Hospitals and clinics: HK rehabilitation experts - Other companies: Vincent Medical Care Holdings Ltd - strategic collaboration with the holding company.	China - direct sales Asia - distributors Russia - distributors Europe - distributors Africa - distributor Middle East - distributors South America - distributor	Equity: $63.859.000 (69%) (a) Debt: $29.212.000 (31%) * a) Consolidated Financial Statements of Vincent Medical Holdings Ltd., FY ended 31/12/2022	$81.353.000	-$2.228.000	13,789%		4646

GUANGZHOU YIKANG MEDICAL EQUIPMENT INDUSTRIAL CO., LTD.	B2B	- Universities and research centers: Zhengzhou University Hangzhou Dianzi University - Hospitals and clinics: Shanghai [...] Hospital Wuhu No.1 People's Hospital Taihe County People's Hospital Central Hospital of ZiBo Jiangzhou Province Official Hospital Zhengzhou Central Hospital Xiangyang Central Hospital Beijing United Family Hospital The First People's Hospital of Zunyi	Global clientele	Equity: $1.086.506 (25%) Debt: $3.343.838 (75%) * FY ended 31/12/2016	$6.067.513	-$21.152	1,028%	ISO9001, ISO13485 ; CE Certifications ; **61 effective patents** (73 chinese patents). 13 software products. 25 software copyrights	3250
NEOFECT CO., LTD.	B2B Partially B2C	Several clinical and business partners in the US, Europe (Germany), and Asia (Korea) [Some] Clinical partners: - NYU Langone Medical Center - Stanford Health Care - Swedish - Department of Veterans Affairs - Vanderbilt University - Medical Center - Brooks Rehabilitation - Genesis - MedStar Health - Rehab at Home - Therapy and nursing services - University of Wisconsin	34 countries (3,284 hospitals)	Equity: $5.117.000 (13%) Debt: $34.630.000 (87%) * FY ended 31/12/2022	$20.675.000	- $7.592.000	3,504%	8 patents	3250

MOTEK MEDICAL B.V.	B2B	- Universities University of Strathclyde, Glasgow Orthopaedic Research Institute, Bournemouth University Melbourne School of Engineering, Melbourne University - University Hospitals VU University, Medical center Amsterdam - Rehabilitation Centers Cleveland Clinic, Rehabilitation Virtual Reality Lab Ottawa Hospital Rehab Centre Brain and Spinal Injury Centre - Sport Institutes - Military Installations Military Rehab Centre Aardenburg - Other companies: DIH Medical Group - holding company	Hub-and-spoke business model Local hubs present in (countries): The Netherlands (EU) Germany (EU) Slovenia (EU) China (Asia) Singapore (Asia) US (Americas) Chile (Americas) Network of distributors in (regions): 13 in EU 1 Ukraine 1 Russia 6 Middle East 7 Asia 3 South America	Equity: $199.259.025 (96.1%) Debt: $8.096.578 (3.9%) * b) Annual Report of DIH Medical Group, FY ended 31/12/2022	$55.000.000	$6.604.155	9,32%		7219
HOCOMA MEDICAL GMBH	B2B B2C	- Hospitals and clinics: CEN, a specialized neurorehabilitation clinic TRAINM, a neurorehabilitation clinic group Ignite Medical Resorts	APAC region - distributors Europe - distributors Americas - distributors	Equity: $199.259.025 (96.1%) Debt: $8.096.578 (3.9%) * b) Annual Report of DIH Medical Group, FY ended 31/12/2022	$55.000.000	$6.604.155	9,32%		3250
HIWIN TECHNOLOGIES CORP.	B2B	- Universities and research centers: China Medical University - Hospitals and clinics: Hospital of Sun Yat-Sen Medical University	Taiwan (5% of sales) Asia (64% of sales) Europe (26% of sales) America (5% of sales)	Equity: $1.142.487.000 (68%) Debt: $531,071,000 (32%) * FY ended 31/12/2023	$806.229.000	$66.203.000	136,649%	Out of 403, **85** patents related to medical robots	2594

MOVENDO TECHNOLOGY S.R.L.	B2B	- Hospitals and cilinics: Several national and international rehab centers - Scientific collaborations: Dompè Holdings IIT - Istituto Italiano di Tecnologia	Italy (Europe) Germany (Europe) Czech Republic (Europe) France (Europe) Spain (Europe) Slovenia (Europe) Greece (Europe) Austria (Europe) Poland (Europe) Switzerland Ukraine US (Americas) Panama (Americas) Canada (Americas) Saudi Arabia (Middle East)	Equity: $1.935.341 (33%) Debt: $3.954.463 (67%) * FY ended 31/12/2022	$2.477.323	$2.973.038	0,42%		
EMAC S.R.L.	B2B		Italy	Equity: $232.942 (8%) Debt: $2.717.716 (92%) * FY ended 31/12/2022	$9.144.665	$11.629	1,559%		4531
HUMANWARE S.R.L.	B2B	- Universities and research centers: Scuola Superiore Sant'Anna (the company is a spin-off) - Other companies: Kiwa NV Rina Services S.p.A.	Italy Some devices have been adopted also in: Spain Qatar	Equity: $277.668 (23%) Debt: $935.400 (77%) * FY ended 31/12/2022	$686.446	$37.985	0,116%	Several R&D projects	7219
REWALK ROBOTICS LIMITED	Global + USA Germany Israel		Corporate Locations are present in: US Germany Israel Distributors are present in: US (Americas) Argentina (Americas) France (Europe) Poland (Europe) Hungary (Europe) Turkey (Middle East) Russia Japan (Asia) Singapore (Asia) Taiwan (Asia) China (Asia) New Zealand	Equity: $46.510.000 (74%) Debt: $16.682.000 (26%) * FY ended 31/12/2023	$13.854.000	- $22.133.000	2,348%		3250
EKSO BIONICS HOLDINGS, INC.	B2B		North America - direct sales Europe - distributors Middle East - distributors APAC - distributors	Equity: $ 12.606.000 (44%) Debt: $ 16.312.000 (56%) * FY ended 31/12/2023	$13.279.000	- $15.198.000	2,251%	24 patents	4690

TYROMOTION GmbH	B2B B2C		Local hubs present in : Austria USA Germany Switzerland Distributors ("more than 55") are present in: North America South America Europe Middle East Russia Asia Oceania	Equity: -$59.000 (0.59%) Debt: $9.957.000 (99.41%) * FY ended 31/03/2023	$14.000.000	- $1.501.000	2,373%		3314
MEDIMEC INTERNATIONAL S.R.L.			Italy - 16 agents covering the country	Equity: $240.833 Debt: $2.276.092	$3.573.881	$45.295	0,606%		4646
IUVO Srl	B2B	- Universities and research centers: Scuola Superiore Sant'Anna (the company is a spin-off) - Other companies: COMAU Össur Participation to several European Projects	Össur is responsible for bringing exoskeleton devices to the market.	Equity: $3.740.210 Debt: $1.018.602	$2.515.119	$199.689	0,426%		7112

NACE: 2660 - Manufacture of electronic medical equipment; 6202 - Consultancy in information technology; 4646 - Wholesale of pharmaceutical goods; 3250 - Manufacture of medical devices; 7219 - Other research and experimental development on natural sciences and engineering; 2594 - Manufacture of fasteners and screw machine products; 4531 - Wholesale trade services of motor vehicle parts and accessories; 4690 - Wholesale of miscellaneous products; 3314 - Repair of industrial electrical machinery and equipment; 7112 - Engineering activities, technical consultancy.